



STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 10/681827

TO: Marcela Cordero Garcia
Location: 3c35 3c18
Monday, March 28, 2005

1654

Case Serial Number: 10/681827

From: Paul Schulwitz
Location: Biotech-Chem Library
REM-1A65
Phone: 571-272-2527

paul.schulwitz@uspto.gov

Search Notes

Scientific and Technical Information Center
SEARCH REQUEST FORM

Requester's Full Name: MARCELA M CORDERO GARCIA Examiner #: 80381 Date: 3/12/05
 Art Unit: 1654 Phone Number: 2-2939 Serial Number: 101681, B27
 Location (Bldg/Room#): REN 3C95 (Mailbox #): 3C18 Results Format Preferred (circle): PAPER DISK

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: DIPEPTIDE PHENYL ETHERS

Inventors (please provide full names): S B E BID DATA SHEET

Earliest Priority Date: 10/7/03

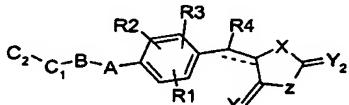
Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

PLEASE SEARCH COMPOUND OF FORMULA I, WHERE:

Novel dipeptide phenyl ethers of formula (I)



(WITH): X=S; Z=NH; Y2=O; Y1=O; R1, R2, R3 and R4=H; --- is absent; A=O; B=p-phenyl; C1=NH-CH(CO2CH3)-CH2-; and C2=the amino acid histidine bonded through the carboxyl end.



IF NO HITS PLEASE SEARCH
BROAD CLM 1



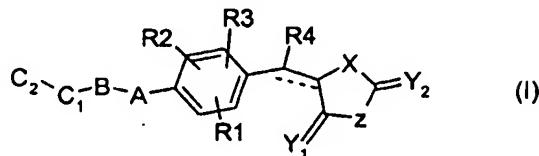
PLEASE SEARCH NPL & MAPPAT

THANKS,
Marcela

STAFF USE ONLY		Type of Search	Vendors and cost where applicable	
Searcher:		NA Sequence (#)	70065 STN	Dialog
Searcher Phone #:		AA Sequence (#)	Questel/Orbit	Lexis/Nexis
Searcher Location:		Structure (#)	Westlaw	WWW/Internet
Date Searcher Picked Up:		Bibliographic	In-house sequence systems	
Date Completed:	<u>3/28</u>	Litigation	Commercial	Score/Length
Searcher Prep & Review Time:	<u>15</u>	Fulltext	Interference	SPDI
Online Time:	<u>15</u>	Other	Other (specify)	

Claims:

1. Novel dipeptide phenyl ethers of formula (I)



their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs,

5 their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates, wherein -- represents an optional double bond; X and Z may be same or different and independently represent oxygen, sulfur or NR₅, wherein R₅ represents hydrogen or linear or branched alkyl group provided both X and Z are not same when they represent oxygen or sulfur. Y₁ and Y₂

10 may be same or different and independently represent oxygen, sulfur or NR₅, wherein R₅ represents hydrogen or linear or branched alkyl group; R₁, R₂, R₃ and R₄ may be same or different and independently represent hydrogen, halogen, hydroxy, nitro, cyano, formyl, mono-, di-, or unsubstituted amino, linear or branched alkyl, linear or branched alkoxy group; A represents oxygen, sulfur or NR, wherein R represents hydrogen or linear or branched alkyl; B represents a bond or substituted or unsubstituted aryl, heterocyclyl or heteroaryl ring of 5 to 14 carbon and hetero atoms; C₁ and C₂ may be same or different and independently represent an amino acid or a derivative thereof and are linked through -NH- of C₁ and -CO- of C₂, or through -CO- of C₁ and -NH- of C₂; B is directly linked or linked through alkyl or alkylene groups of 1 to 4 carbon atoms to the α -carbon of C₁.

20 2. A compound of formula (I) according to claim 1, wherein the group represented by B is selected from aryl such as phenyl, naphthyl; heteroaryl ring such as pyridyl, pyrrolyl, thiazolyl, indolyl, imidazolyl, furyl; heterocyclyl ring such as piperazine, morpholine, piperidine, pyrrolidine.

25 3. A compound of formula (I) according to claim 1, wherein the amino acids represented by C₁ and C₂ are selected from alanine, glycine, arginine, asparagine, cysteine, cystine, glutamic acid, glutamine, histidine, isoleucine, leucine, lysine, methionine, ornithine, proline, serine, threonine, tryptophan, tyrosine or their derivatives.

4. A compound according to claim 3 wherein C₁ and C₂ are linked through -NH- of C₁ and -CO- of C₂.

30 5. A compound according to claim 3 wherein C₁ and C₂ are linked through -CO- of C₁ and -NH- of C₂.



STIC SEARCH RESULTS FEEDBACK FORM

Biotech-Chem Library

Questions about the scope or the results of the search? Contact **the searcher or contact:**

Mary Hale, Information Branch Supervisor
Remsen Bldg. 01 D86
571-272-2507

Voluntary Results Feedback Form

➤ *I am an examiner in Workgroup:* *Example: 1610*

➤ *Relevant prior art found, search results used as follows:*

- 102 rejection
- 103 rejection
- Cited as being of interest.
- Helped examiner better understand the invention.
- Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- Foreign Patent(s)
- Non-Patent Literature
(journal articles, conference proceedings, new product announcements etc.)

➤ *Relevant prior art not found:*

- Results verified the lack of relevant prior art (helped determine patentability).
- Results were not useful in determining patentability or understanding the invention.

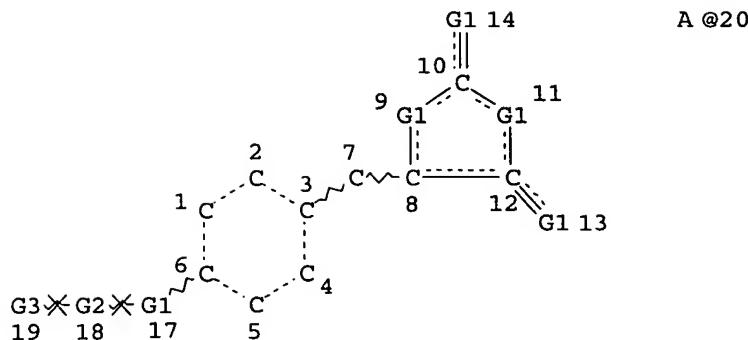
Comments:

Drop off or send completed forms to STIC-Biotech-Chem Library Remsen Bldg.



=> d que 17

L3 STR

N~Ak
@15 16NH~C~C=O
@21 22 @23 24

VAR G1=O/S/NH/15

REP G2=(0-10) 20

VAR G3=21/23

NODE ATTRIBUTES:

NSPEC IS RC AT 20

CONNECT IS E1 RC AT 16

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE

L5 107 SEA FILE=REGISTRY SSS FUL L3

L6 42 SEA FILE=REGISTRY ABB=ON PLU=ON L5/COM

L7 10 SEA FILE=HCAPLUS ABB=ON PLU=ON L6

=>d 17 bib abs hitstr 1-10

L7 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:780554 HCAPLUS

DOCUMENT NUMBER: 141:301422

TITLE: Preparation of heterocyclic ligands for acid-stabilized insulin analogs

INVENTOR(S): Ostergaard, Soren; Olsen, Helle Birk; Kaarsholm, Niels C.; Madsen, Peter; Jakobsen, Palle; Ludvigsen, Svend; Schluckebier, Gerd; Steensgaard, Dorte Bjerre; Petersen, Anders Klarskov

PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.

SOURCE: PCT Int. Appl., 473 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004080480	A1	20040923	WO 2004-DK158	20040311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			DK 2003-365	A 20030311
			US 2003-455400P	P 20030317

OTHER SOURCE(S): MARPAT 141:301422

AB Novel ligands for the His-B10 Zn²⁺ sites of the R-state insulin hexamer that are capable of prolonging the action of insulin prepns. are disclosed. A mixture of 4-aminobenzonitrile, sodium azide and ammonium chloride in DMF was heated at 125° for 16 h. The cooled mixture was filtered and the filtrate was concentrated to give 5-(4-aminophenyl)-2H-tetrazole. This was used as the ligand for His-B10 Zn²⁺ sites of the R-state insulin hexamer.

IT 503829-76-3P 503829-77-4P 503829-78-5P
503829-79-6P 503829-80-9P 503829-81-0P
503829-82-1P 503829-83-2P 762267-92-5P

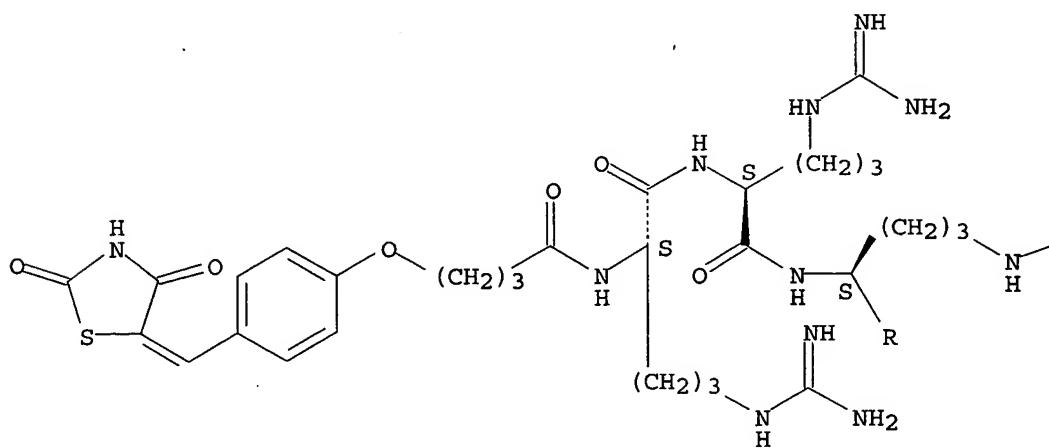
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic ligands for acid-stabilized insulin analogs)

RN 503829-76-3 HCAPLUS

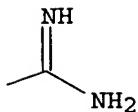
CN L-Argininamide, N2-[4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]-1-oxobutyl]-L-arginyl-L-arginyl-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

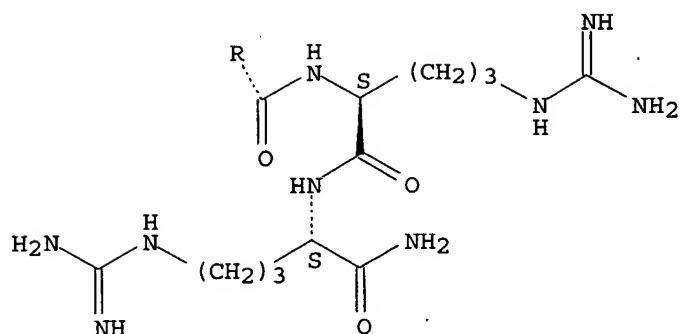
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PAGE 1-B



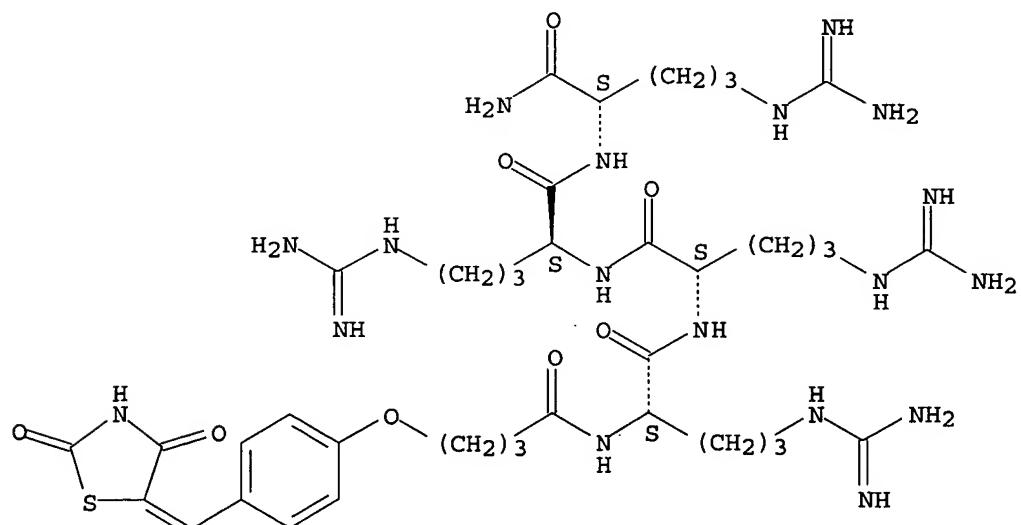
PAGE 2-A



RN 503829-77-4 HCPLUS

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Absolute stereochemistry.
Double bond geometry unknown.

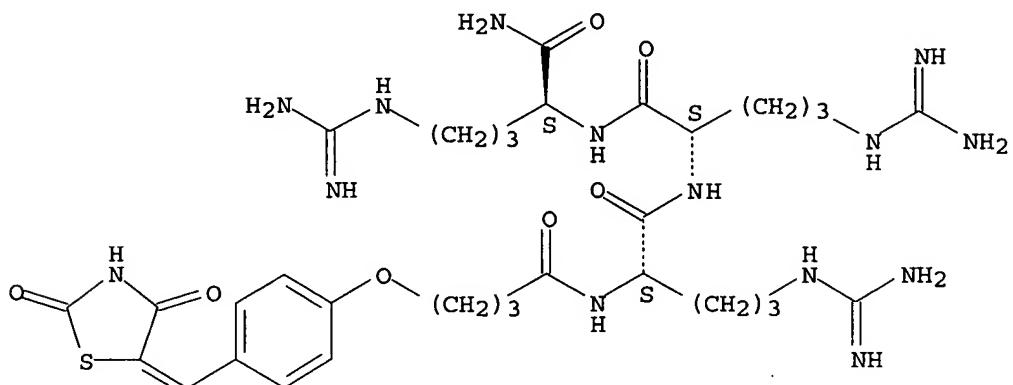


RN 503829-78-5 HCAPLUS

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Absolute stereochemistry.

Double bond geometry unknown.

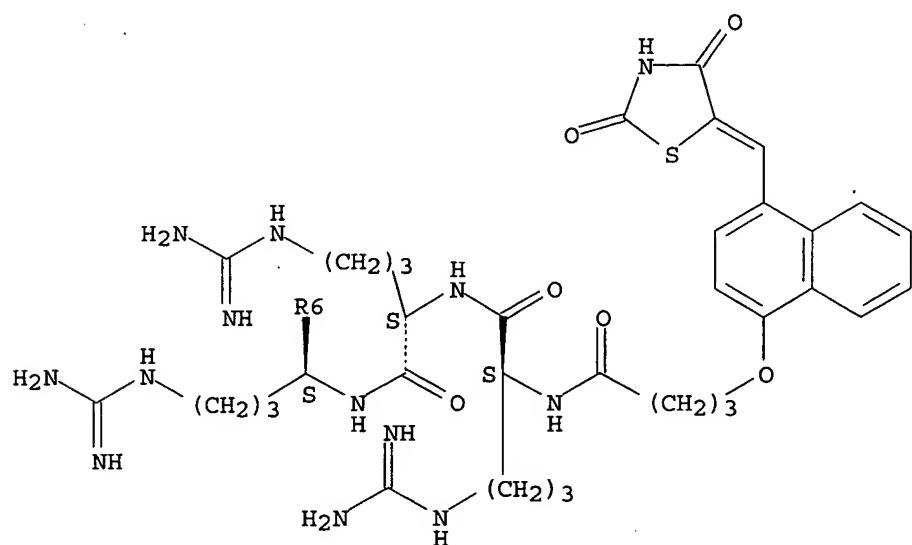


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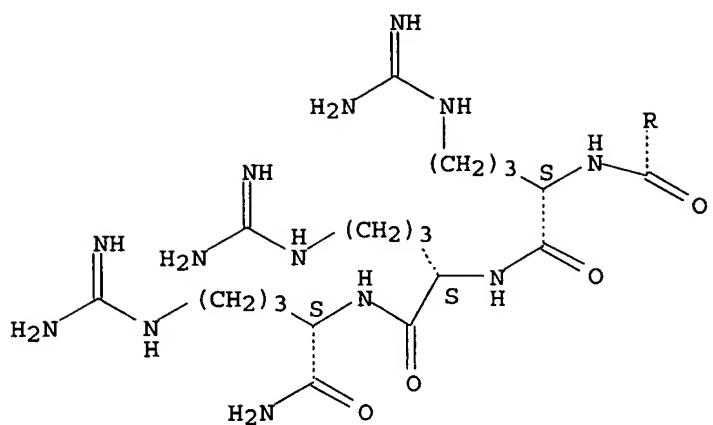
Absolute stereochemistry.

Absolute stereochemistry.
Double bond geometry unknown.

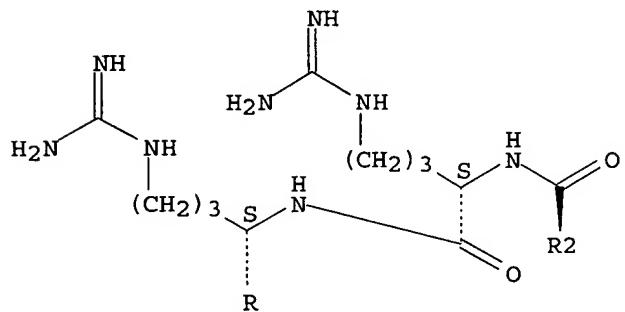
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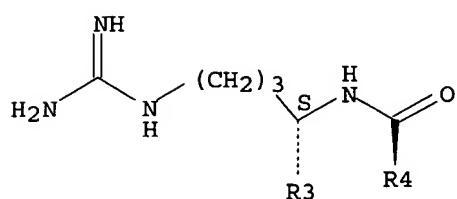
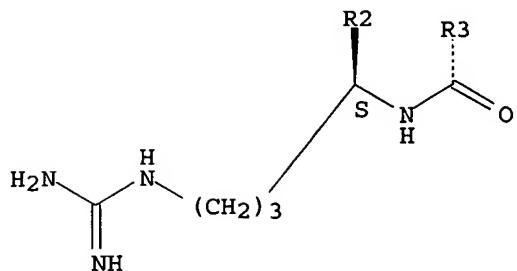
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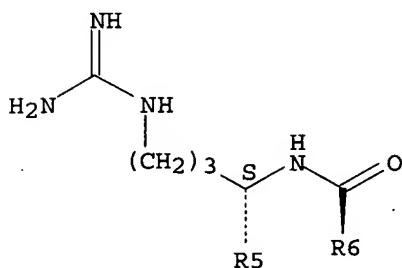
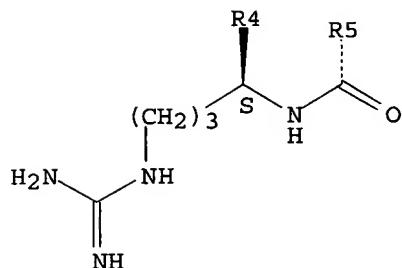
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PAGE 4-A



PAGE 5-A

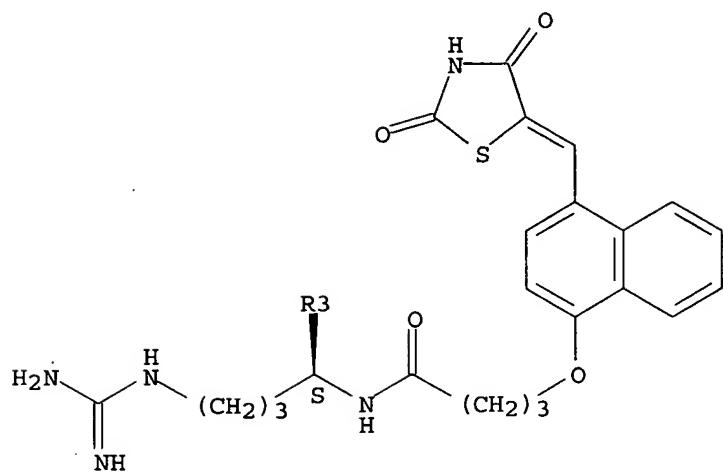


RN 503829-80-9 HCPLUS

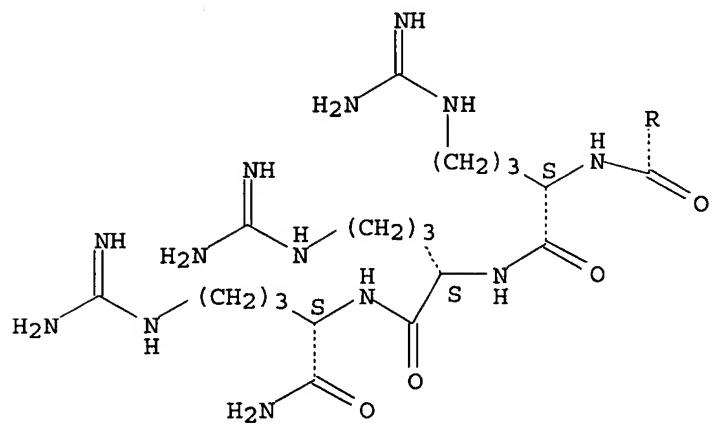
CN L-Argininamide, N2-[4-[[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]-1-naphthalenyl]oxy]-1-oxobutyl]-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

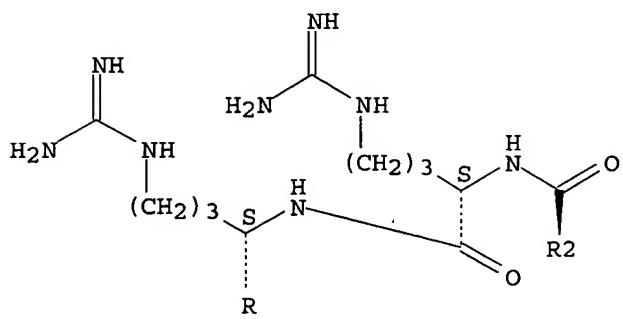
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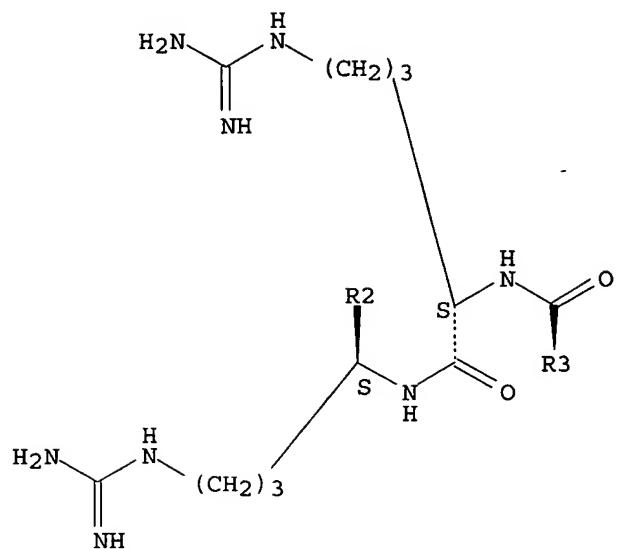
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PAGE 3-A



PAGE 4-A



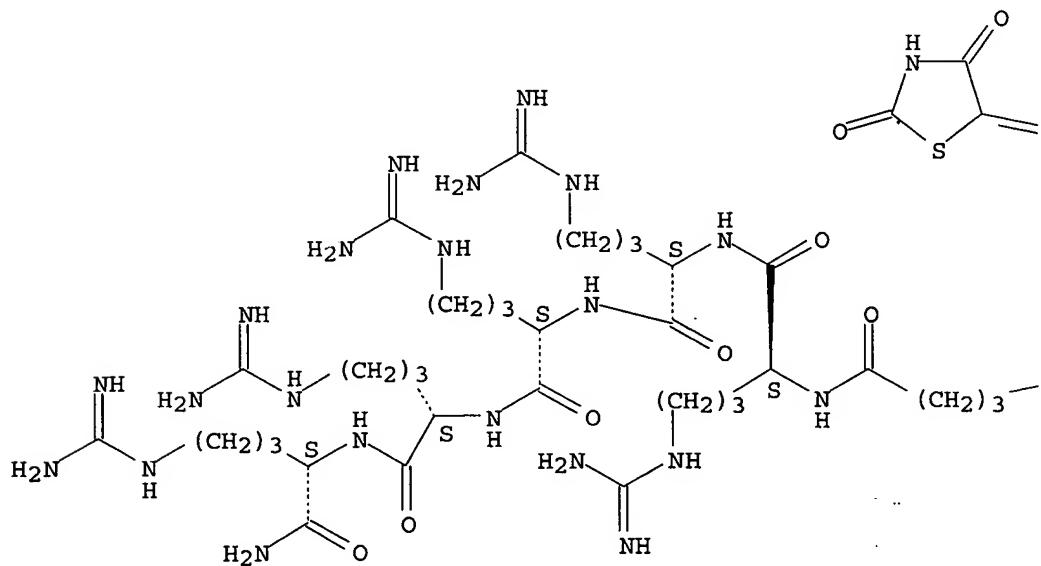
RN 503829-81-0 HCPLUS

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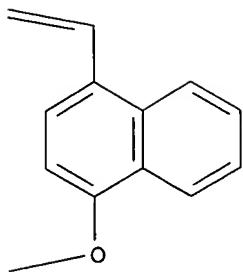
Absolute stereochemistry.

Double bond geometry unknown.

PAGE 1-A



PAGE 1-B

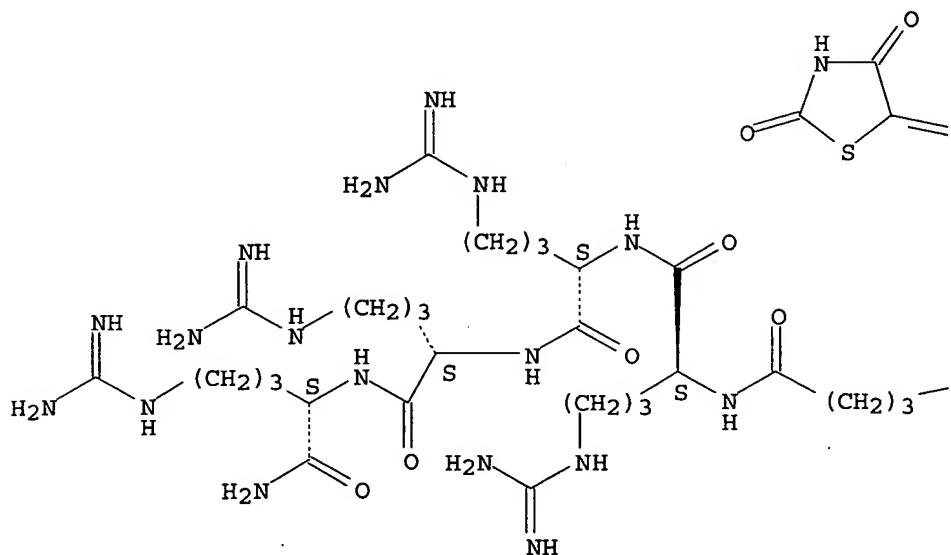


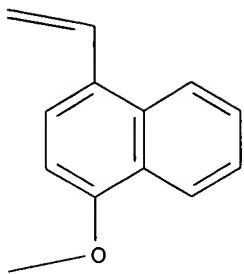
RN 503829-82-1 HCAPLUS

CN L-Argininamide, N2-[4-[[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]-1-naphthalenyl]oxy]-1-oxobutyl]-L-arginyl-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

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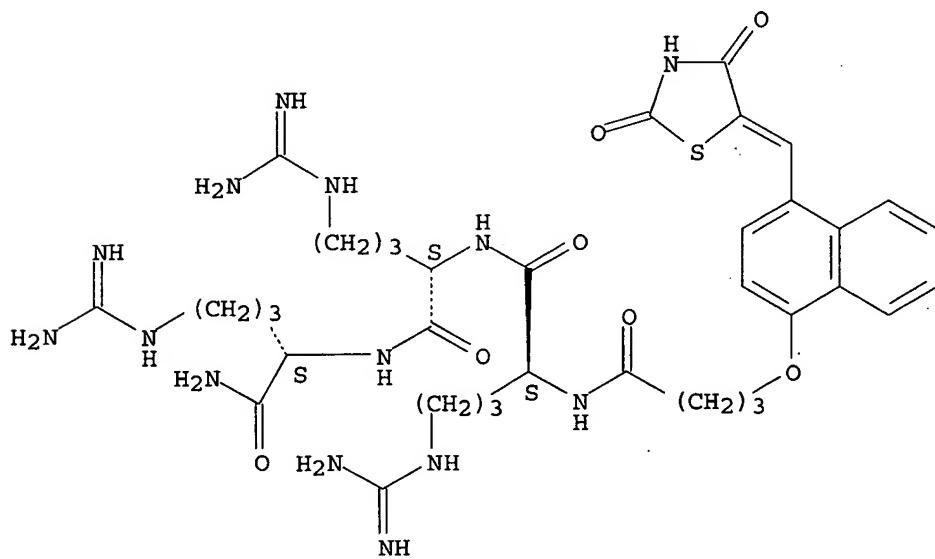


RN 503829-83-2 HCPLUS

CN L-Argininamide, N2-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]-1-naphthalenyl]oxy]-1-oxobutyl-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



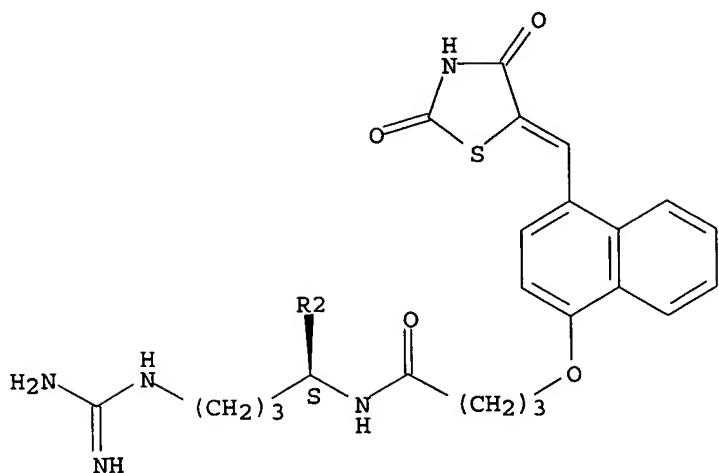
RN 762267-92-5 HCPLUS

CN L-Argininamide, N2-[4-[(2,4-dioxo-4-thiazolidinylidene)methyl]-1-naphthalenyl]oxy]-1-oxobutyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

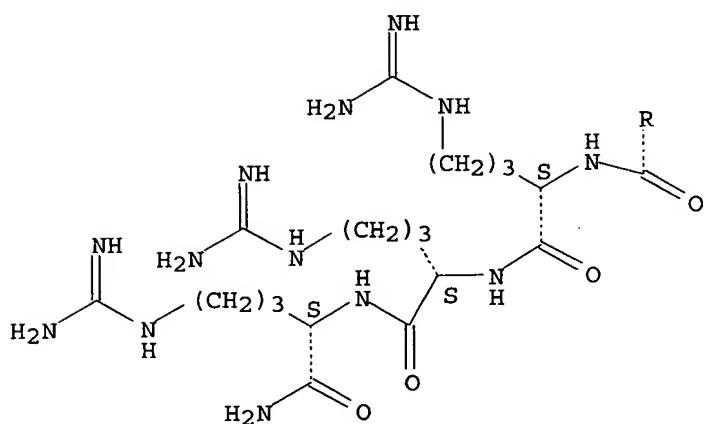
Absolute stereochemistry.

Double bond geometry unknown.

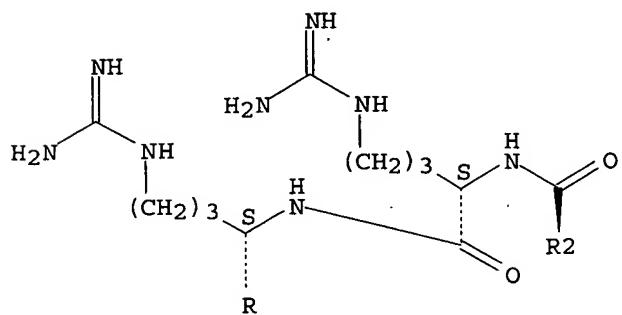
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PAGE 2-A



PAGE 3-A

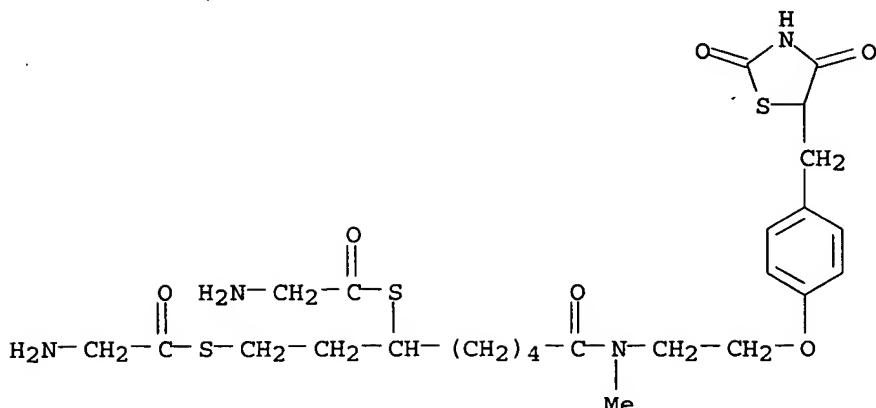


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2004:674192 HCAPLUS
 DOCUMENT NUMBER: 142:169368
 TITLE: α -Lipoic acid-based PPAR γ agonists for treating inflammatory skin diseases
 AUTHOR(S): Venkatraman, Meenakshi S.; Chittiboyina, Amar; Meingassner, Josef; Ho, Christopher I.; Varani, James; Ellis, Charles N.; Avery, Mitchell A.; Pershadsingh, Harrihar A.; Kurtz, Theodore W.; Benson, Stephen C.
 CORPORATE SOURCE: Department Medicinal Chemistry, University of Mississippi, University, MS, USA
 SOURCE: Archives of Dermatological Research (2004), 296(3), 97-104
 CODEN: ADREDL; ISSN: 0340-3696
 PUBLISHER: Springer GmbH
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Novel thiazolidinedione derivs. of the potent antioxidant, α -lipoic (thioctic, 1,2-dithiolane) acid, were prepared. The prototype N-(2-{4-[2,4-dioxo(1,3-thiazolidin-5-yl)methyl]phenoxy}ethyl)-5-(1,2-dithiolan-3-yl)-N-methylpentanamide (designated BP-1003), and dithioester derivs. thereof were shown to be potent activators of peroxisome proliferator-activated receptor gamma (PPAR γ) (EC50 range 15-101 nM) and modest activators of PPAR α (EC50 5 μ M). Both the relatively hydrophobic dithiolane prototype, BP-1003, and its water-soluble dithioglycinate derivative, BP-1017, were shown to inhibit the proliferation of human keratinocytes and suppress the production of interleukin-2 by human peripheral lymphocytes to a greater extent than the antidiabetic thiazolidinedione, rosiglitazone. Both oral and topical administration of BP-1017 showed significant antiinflammatory effects in the oxazolone-sensitized mouse model of allergic contact dermatitis (ACD). These findings suggest that water-soluble lipoic acid-based thiazolidinediones may be efficacious as oral and topical agents for treating inflammatory skin conditions such as contact dermatitis, atopic dermatitis, and psoriasis.

IT 835650-57-2, BP 1017
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (BP-1017 strongly activated PPAR γ , modestly activated PPAR α in CCL-70 cells and activated PPAR γ in CCL-173 cells, inhibited proliferation of human keratinocytes and IL-2 production by activated PBMC than rosiglitazone)
 RN 835650-57-2 HCAPLUS
 CN Ethanethioic acid, amino-, S,S'-[1-[5-[[2-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]ethyl]methylamino]-5-oxopentyl]-1,3-propanediyl] ester, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:566933 HCAPLUS

DOCUMENT NUMBER: 141:270985

TITLE: Three-Dimensional Quantitative Structure-Activity Relationship Analysis of a Set of Plasmodium falciparum Dihydrofolate Reductase Inhibitors Using a Pharmacophore Generation Approach

AUTHOR(S): Parenti, Marco Daniele; Pacchioni, Sara; Ferrari, Anna Maria; Rastelli, Giulio

CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Modena e Reggio Emilia, Modena, 41100, Italy

SOURCE: Journal of Medicinal Chemistry (2004), 47(17), 4258-4267

CODEN: JCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

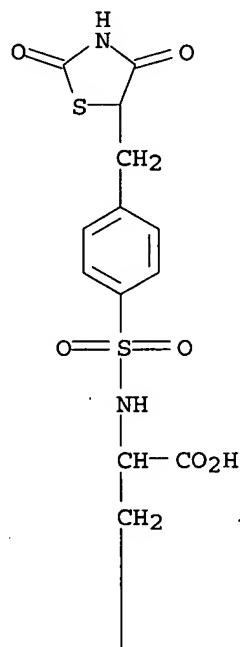
AB A 3D pharmacophore model able to quant. predict inhibition consts. was derived for a series of inhibitors of Plasmodium falciparum dihydrofolate reductase (PfDHFR), a validated target for antimalarial therapy. The data set included 52 inhibitors, with 23 of these comprising the training set and 29 an external test set. The activity range, expressed as Ki, of the training set mols. was from 0.3 to 11 300 nM. The 3D pharmacophore, generated with the HypoGen module of Catalyst 4.7, consisted of two hydrogen bond donors, one pos. ionizable feature, one hydrophobic aliphatic feature, and one hydrophobic aromatic feature and provided a 3D-QSAR model with a correlation coefficient of 0.954. Importantly, the type and spatial location of the chemical features encoded in the pharmacophore were in full agreement with the key binding interactions of PfDHFR inhibitors as previously established by mol. modeling and crystallog. of enzyme-inhibitor complexes. The model was validated using several techniques, namely, Fisher's randomization test using CatScramble, leave-one-out test to ensure that the QSAR model is not strictly dependent on one particular compound of the training set, and activity prediction in an external test set of compds. In addition, the pharmacophore was able to

correctly classify as active and inactive the dihydrofolate reductase and aldose reductase inhibitors extracted from the MDDR database, resp. This test was performed to challenge the predictive ability of the pharmacophore with two classes of inhibitors that target very different binding sites. Mol. diversity of the data sets was finally estimated by the Tanimoto approach. The results obtained provide confidence for the utility of the pharmacophore in the virtual screening of libraries and databases of compds. to discover novel PfDHFR inhibitors.

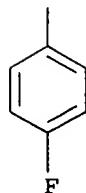
IT 184095-78-1 184095-80-5 184095-82-7
 184095-85-0 756890-15-0 756890-16-1
 756890-17-2
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (QSAR of Plasmodium falciparum dihydrofolate reductase inhibitors using pharmacophore generation approach)

RN 184095-78-1 HCPLUS
 CN Phenylalanine, N-[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]sulfonyl]-4-fluoro- (9CI) (CA INDEX NAME)

PAGE 1-A

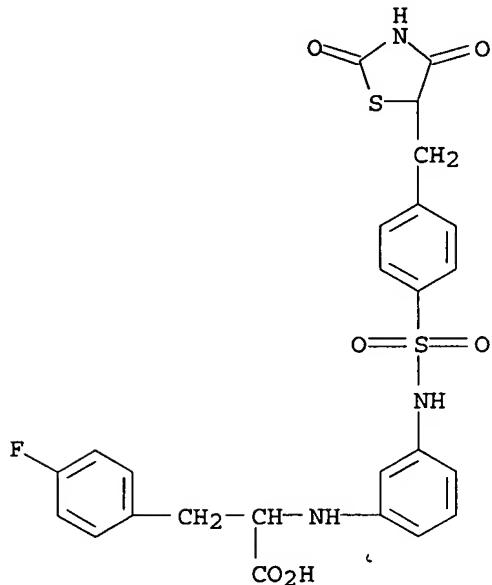


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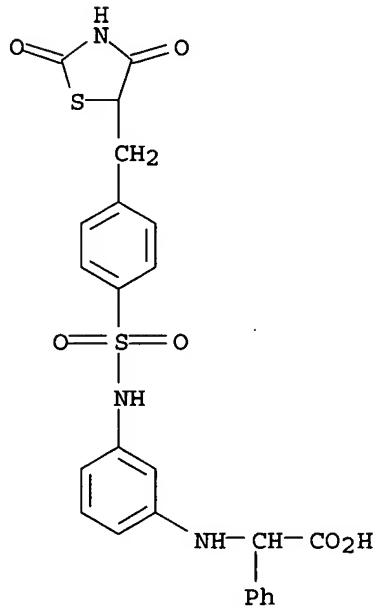


RN 184095-80-5 HCPLUS

CN Phenylalanine, N-[3-[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]sulfonyl]amino]phenyl]-4-fluoro- (9CI) (CA INDEX NAME)

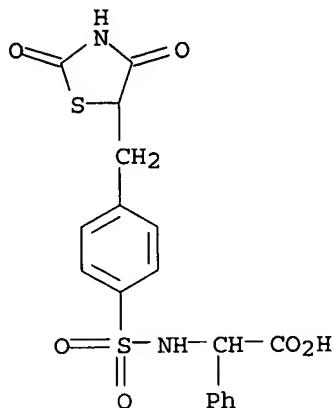


RN 184095-82-7 HCPLUS

CN Benzeneacetic acid, α -[[3-[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]sulfonyl]amino]phenyl]amino]- (9CI) (CA INDEX NAME)

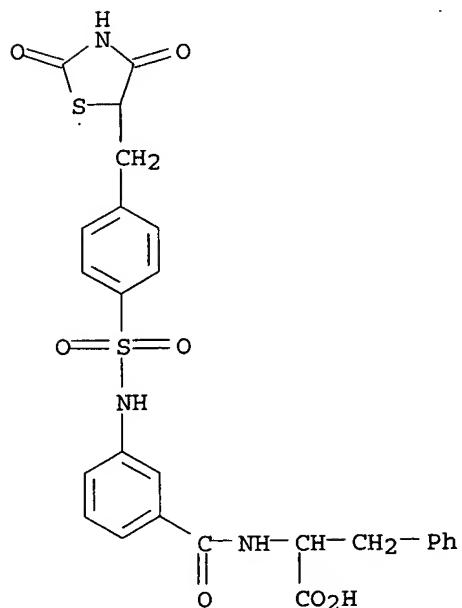
RN 184095-85-0 HCPLUS

CN Benzeneacetic acid, α -{[(4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl)sulfonyl]amino}- (9CI) (CA INDEX NAME)



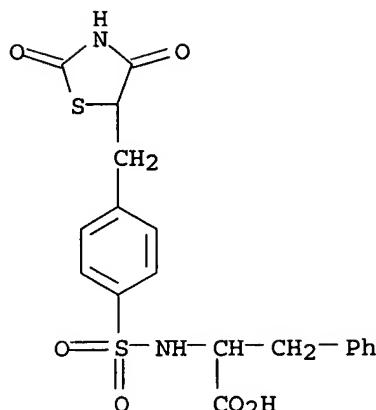
RN 756890-15-0 HCAPLUS

CN Phenylalanine, N-[3-[(4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl)sulfonyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

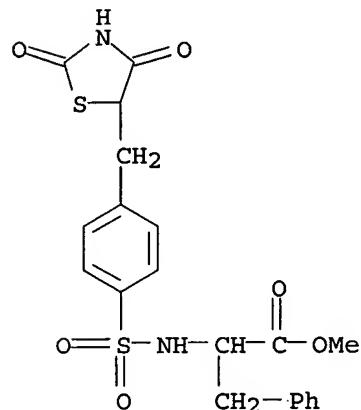


RN 756890-16-1 HCAPLUS

CN Phenylalanine, N-[(4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl)sulfonyl]- (9CI) (CA INDEX NAME)



RN 756890-17-2 HCAPLUS
 CN Phenylalanine, N-[(4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 .ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2003:261820 HCAPLUS
 DOCUMENT NUMBER: 138:287978
 TITLE: Novel ligands for the HisB10 Zn²⁺ sites of the R-state insulin hexamer
 INVENTOR(S): Olsen, Helle Birk; Kaarsholm, Niels C.; Madsen, Peter; Ostergaard, Soren; Ludvigsen, Svend; Jakobsen, Palie; Petersen, Anders Klarskov; Steensgaard, Dorte Bjerre
 PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.; Novo Nordisk Health Care AG
 SOURCE: PCT Int. Appl., 342 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003027081	A2	20030403	WO 2002-DK595	20020913
WO 2003027081	A3	20040325		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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EP 1429763	A2	20040623	EP 2002-774468	20020913
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002012522	A	20040810	BR 2002-12522	20020913
US 2003229120	A1	20031211	US 2003-332541	20030514
PRIORITY APPLN. INFO.:			DK 2001-1337	A 20010914
			US 2001-323925P	P 20010921
			DK 2002-1066	A 20020705
			US 2002-396051P	P 20020710
			WO 2002-DK595	W 20020913

OTHER SOURCE(S): MARPAT 138:287978

AB Novel ligands for the HisB10 Zn²⁺ sites of the R-state insulin hexamer that are capable of prolonging the action of insulin preps. are disclosed. The ligands stabilize the hexamers and modify solubility in the neutral range, thus releasing insulin slowly following s.c. injection. Zinc-binding ligands A-B-C-D-X [A is a group which reversibly binds to a HisB10 Zn²⁺ site of an insulin hexamer; B is a linker selected from a valence bond or a chemical group GB of formula -B1-B2-CO-, -B1-B2-SO2-, -B1-B2-CH2-, or -B1-B2-NH-, where B1 is a valence bond, O, S, NH, or alkylimino and B2 is a valence bond, alk(en)(yn)ylene, (hetero)arylene, alkanedioyl, etc.; C is a fragment consisting of 0-5 neutral amino acids; D is a fragment comprising 1 to 20 pos. charged groups selected from amino or guanidino groups; X is OH, NH₂ or a diamino group], including pharmaceutically-acceptable salts, isomers or racemates, are claimed. Thus, benzotriazol-5-ylcarbonyl-Gly₂-Arg₅-NH₂ (BT-G2R5) was prepared and its effect on the pH-solubility profile of an insulin preparation is shown graphically.

IT 503829-76-3P 503829-77-4P 503829-78-5P
503829-79-6P 503829-80-9P 503829-81-0P
503829-82-1P 503829-83-2P

RL: BCP (Biochemical process); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(novel ligands for histidine-B10 zinc(II) sites of R-state insulin hexamer)

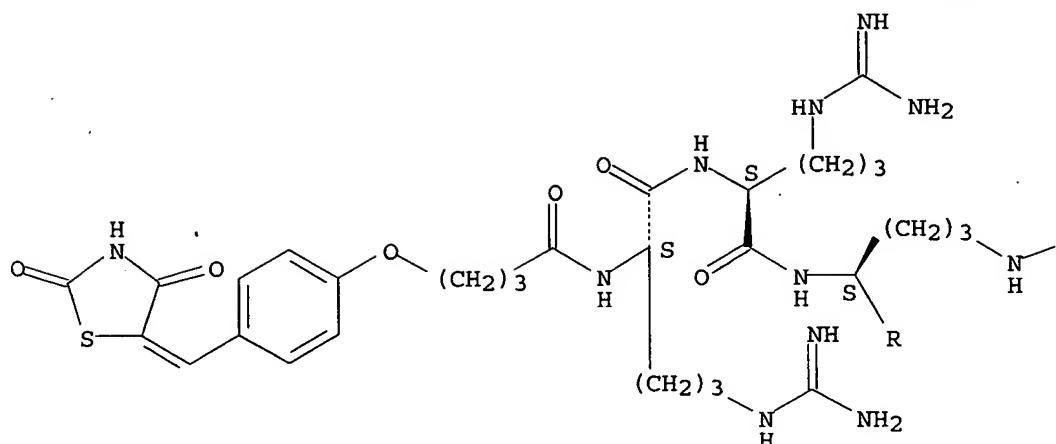
RN 503829-76-3 HCPLUS

CN L-Argininamide, N2-[4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]-1-oxobutyl]-L-arginyl-L-arginyl-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

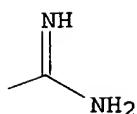
Absolute stereochemistry.

Double bond geometry unknown.

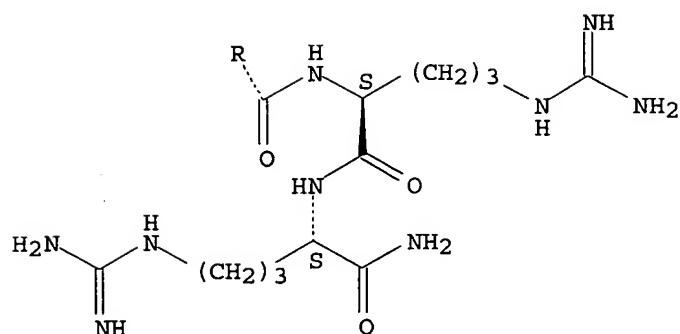
PAGE 1-A



PAGE 1-B



PAGE 2-A

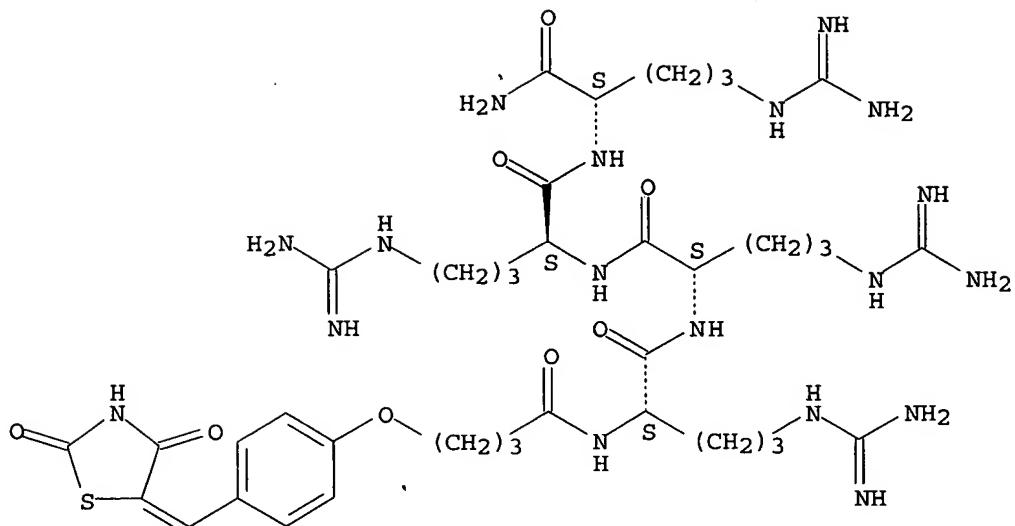


RN 503829-77-4 HCPLUS

CN L-Argininamide, N2-[4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]-1-oxobutyl]-L-arginyl-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

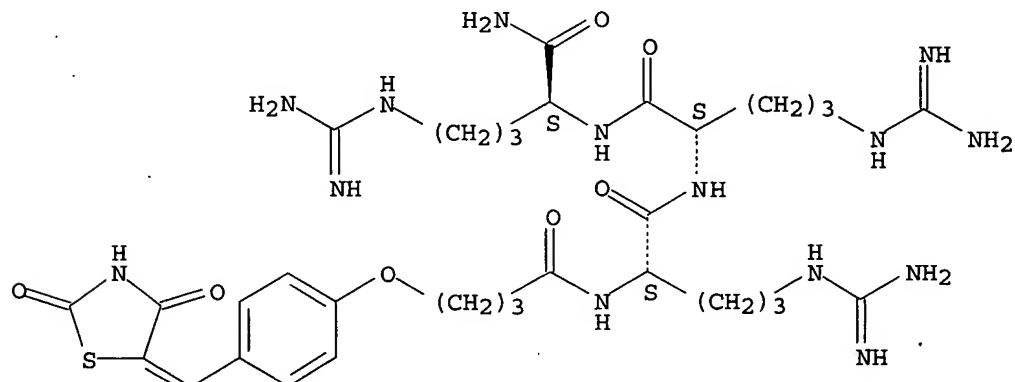


RN 503829-78-5 HCAPLUS

CN L-Argininamide, N2-[4-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]phenoxy]-1-oxobutyl]-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



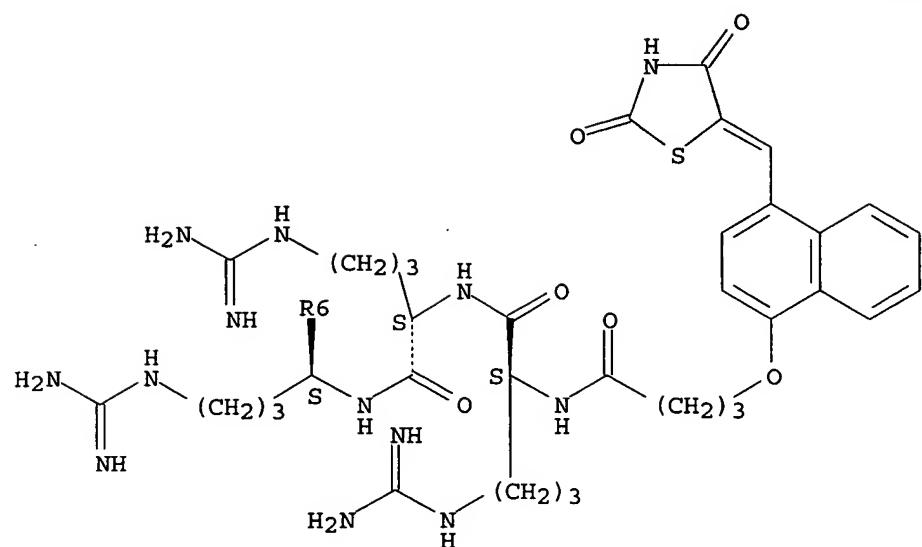
RN 503829-79-6 HCAPLUS

CN L-Argininamide, N2-[4-[[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]-1-naphthalenyl]oxy]-1-oxobutyl]-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

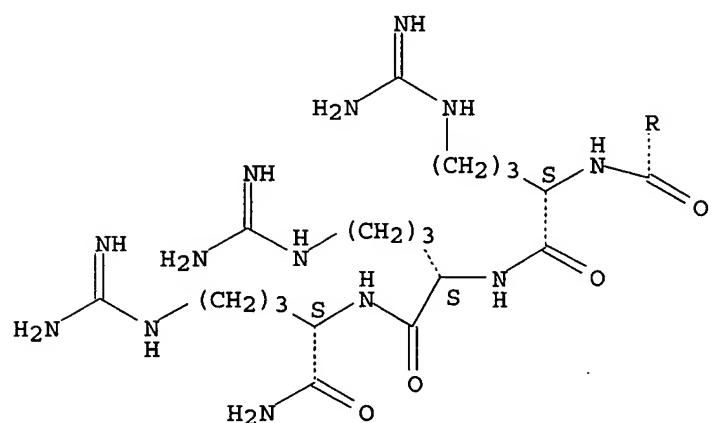
Absolute stereochemistry.

Double bond geometry unknown.

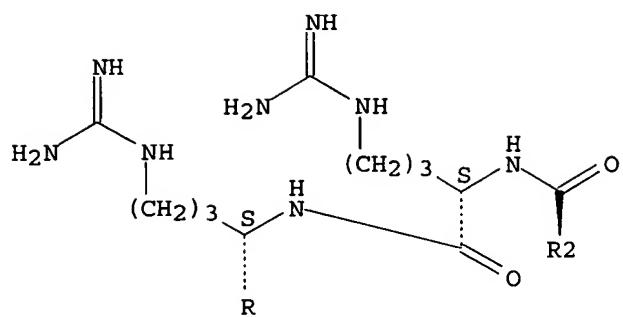
PAGE 1-A



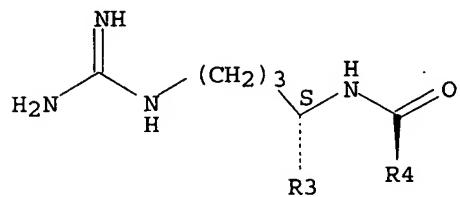
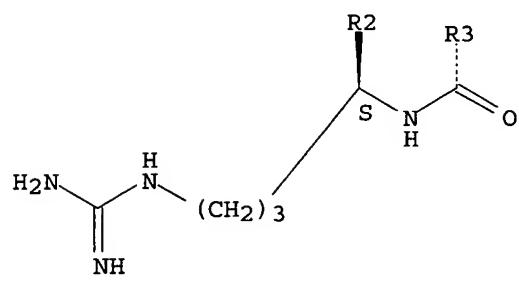
PAGE 2-A



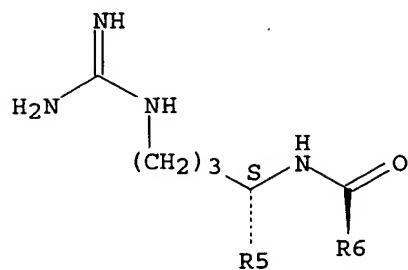
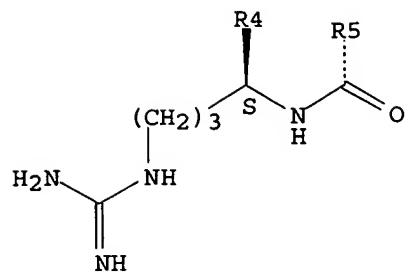
PAGE 3-A



PAGE 4-A



PAGE 5-A



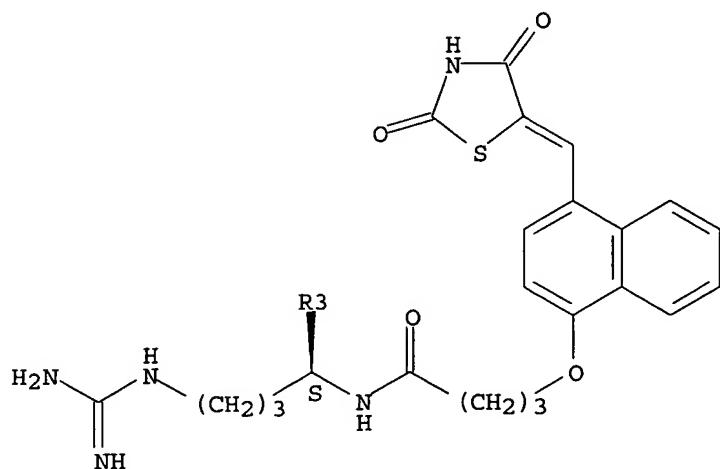
RN 503829-80-9 HCPLUS

CN L-Argininamide, N2-[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]-1-naphthalenyl]oxy]-1-oxobutyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

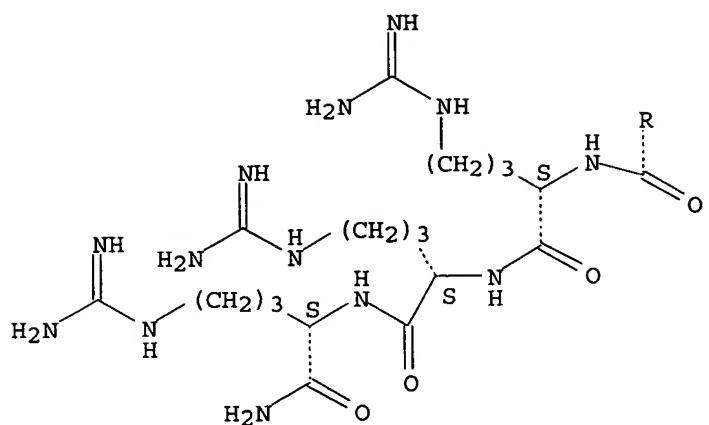
Absolute stereochemistry.

Double bond geometry unknown.

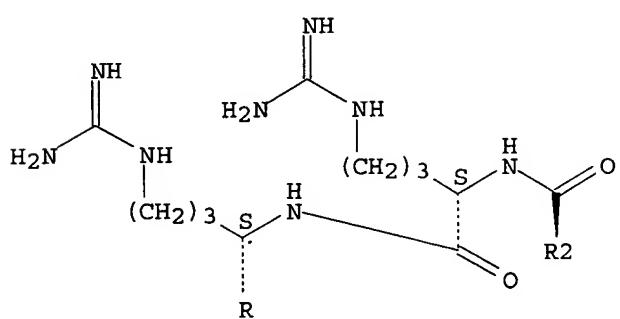
PAGE 1-A



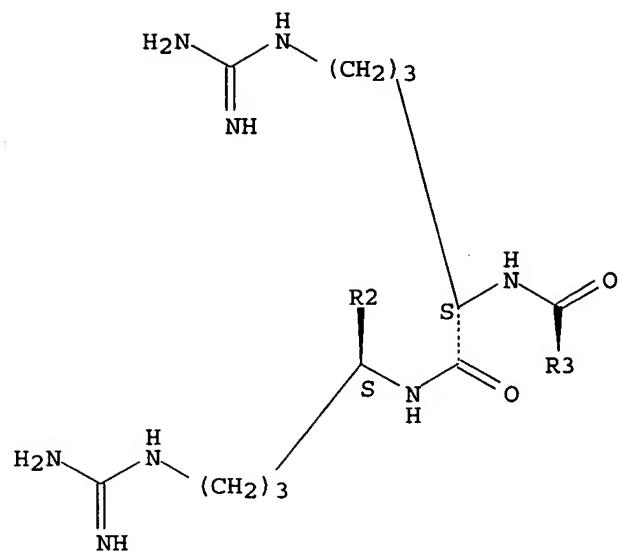
PAGE 2-A



PAGE 3-A



PAGE 4-A

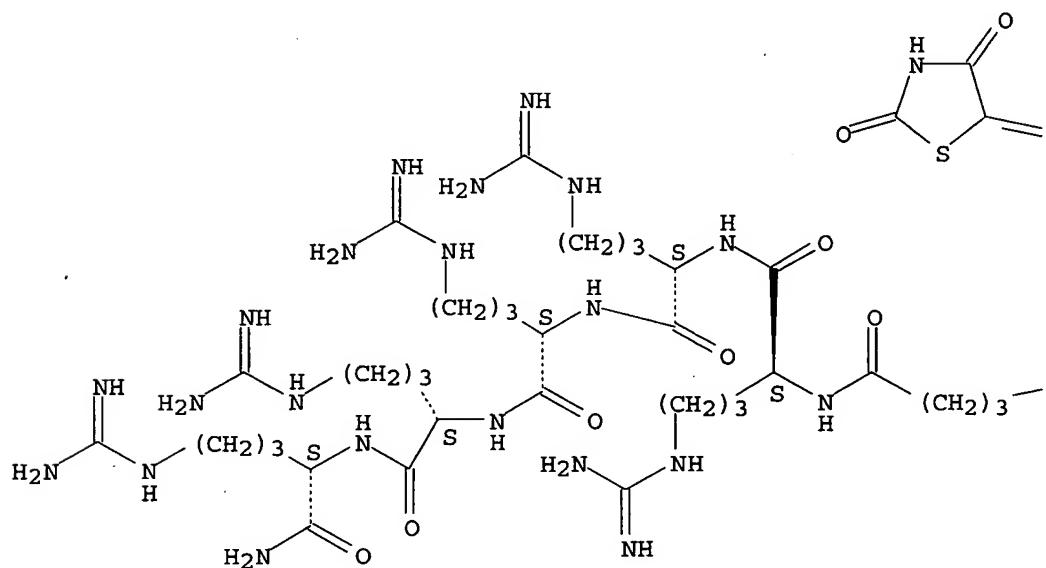


RN 503829-81-0 HCAPLUS

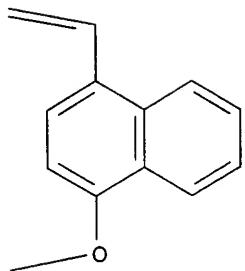
CN L-Argininamide, N2-[4-[[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]-1-naphthalenyl]oxy]-1-oxobutyl]-L-arginyl-L-arginyl-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

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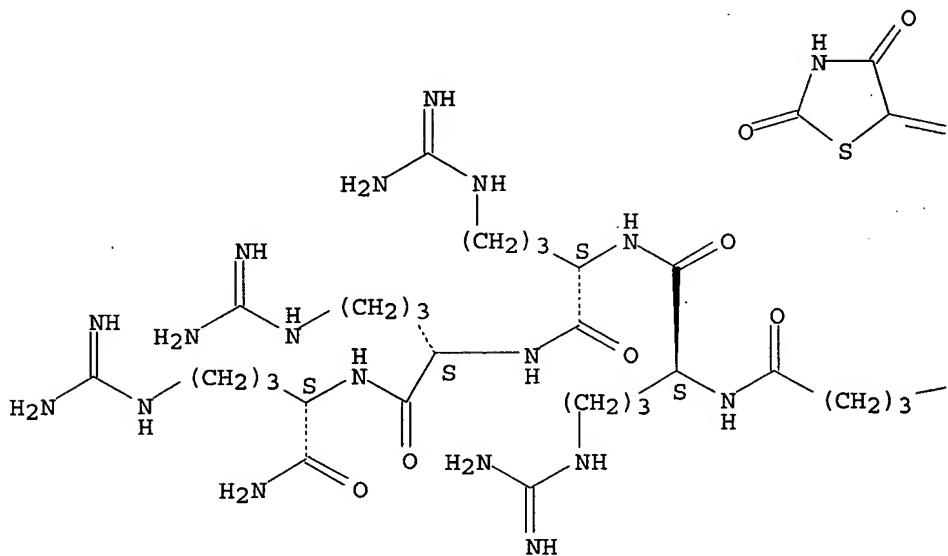


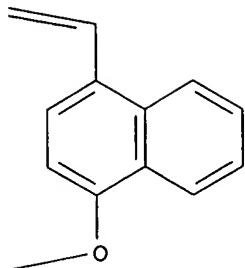
RN 503829-82-1 HCAPLUS

CN L-Argininamide, N2-[4-[[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]-1-naphthalenyl]oxy]-1-oxobutyl]-L-arginyl-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



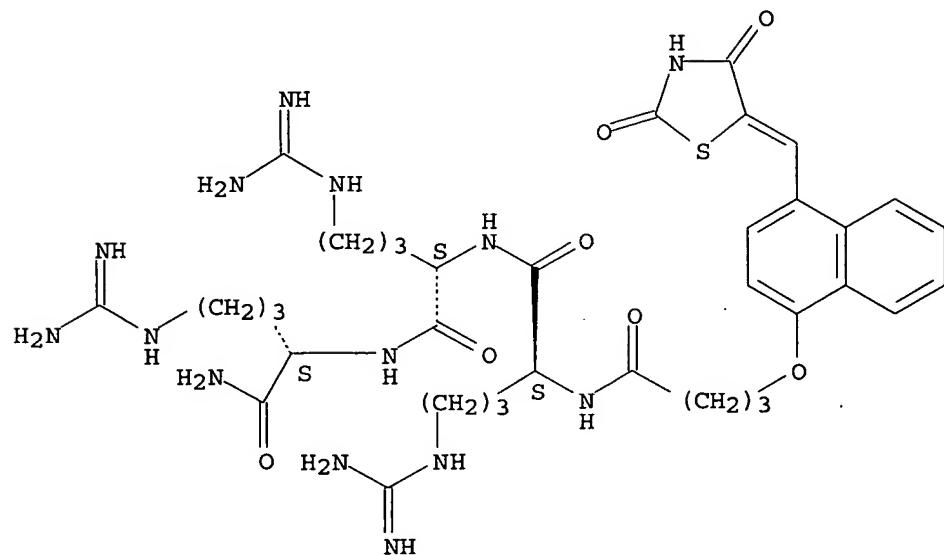


RN 503829-83-2 HCAPLUS

CN L-Argininamide, N2-[4-[[4-[(2,4-dioxo-5-thiazolidinylidene)methyl]-1-naphthalenyl]oxy]-1-oxobutyl]-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



L7 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:479961 HCAPLUS

DOCUMENT NUMBER: 137:41755

TITLE: Antidiabetic agents containing amine derivatives having benzimidazole or imidazopyridine ring and their other uses

INVENTOR(S): Fujita, Takashi; Wada, Kunio; Oguchi, Minoru; Honma, Eiji; Fujiwara, Toshihiko

PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan

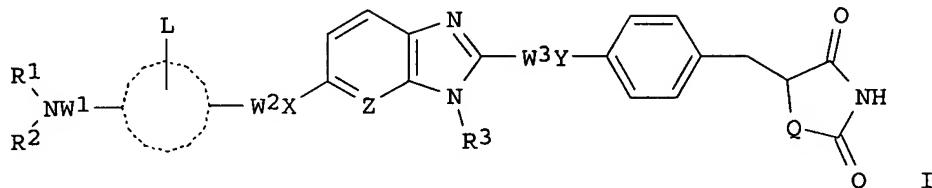
SOURCE: Jpn. Kokai Tokkyo Koho, 109 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002179568	A2	20020626	JP 2001-308814	20011004
PRIORITY APPLN. INFO.:			JP 2000-307159	A 20001006
OTHER SOURCE(S):	MARPAT 137:41755			
GI				



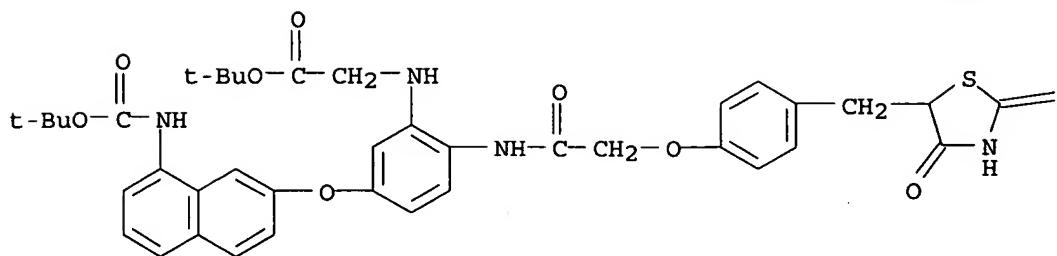
AB Prophylactic and/or therapeutic agents for diabetes, glucose intolerance, diabetic complications, or gestational diabetes contain the derivs. I (R1 = carbamoyl which may have 1-2 α , thiocarbamoyl which may have 1-2 α , sulfonyl having 1 α , carbonyl having 1 α ; R2, R3 = H, C1-10 alkyl, C6-10 aryl, which may have 1-3 β , C7-16 aralkyl which may have 1-3 β on the aryl moiety; W1-W3 = direct bond, C1-8 alkylene; X, Y, Q = O, S; Z = :CH, N' Ar = benzene or naphthalene ring substituted with 1-4 L; L = H, C1-6 alkyl, C6-10 aryl which may have 1-3 β , C7-16 aralkyl which may have 1-3 β on the aryl moiety; definitions of α and β are given) or their pharmacol. acceptable salts. I and their salts are also useful as insulin resistance improving agents, hypoglycemics, inflammation inhibitors, immunomodulators, aldose reductase inhibitors, 5-lipoxygenase inhibitors, lipid peroxide formation inhibitors, PPAR activators, antosteoporotic agents, leukotriene antagonists, adipocyte conversion promoters, cancer cell growth inhibitors, and Ca blockers. Feeding diabetic KK mice with feed containing 0.01% 1-(4-chlorophenyl)-3-[4-[2-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenoxy]methyl]-1-methyl-1H-benzimidazol-6-yloxy]-2,6-dimethylphenylthiourea (II) for 3 days showed 48.9% hypoglycemic effect. Capsules, tablets, and granules containing II were also formulated.

IT 438577-87-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of benzimidazole or imidazopyridine compds. as antidiabetic agents)

RN 438577-87-8 HCAPLUS

CN Glycine, N-[5-[[8-[[[(1,1-dimethylethoxy)carbonyl]amino]-2-naphthalenyl]oxy]-2-[[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]acetyl]amino]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

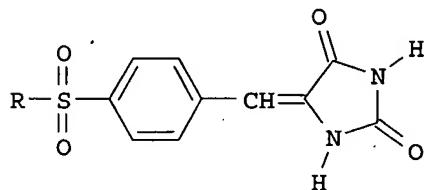
PAGE 1-A



PAGE 1-B

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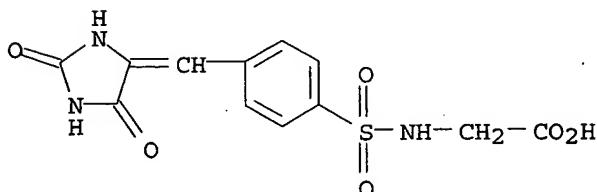
L7 ANSWER 6 OF 10 HCPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2001:493888 HCPLUS
 DOCUMENT NUMBER: 135:242192
 TITLE: Synthesis of some novel benzylidenehydantoins: amino acids derivatives
 AUTHOR(S): El-Sayed, Ragab A.
 CORPORATE SOURCE: Chemistry Department, Faculty of Science, Al-Azhar University, Nasr-City, Egypt
 SOURCE: Chemistry of Heterocyclic Compounds (New York, NY, United States) (Translation of Khimiya Geterotsiklichesikh Soedinenii) (2001), 37(1), 91-94
 CODEN: CHCCAL; ISSN: 0009-3122
 PUBLISHER: Kluwer Academic/Consultants Bureau
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 135:242192
 GI



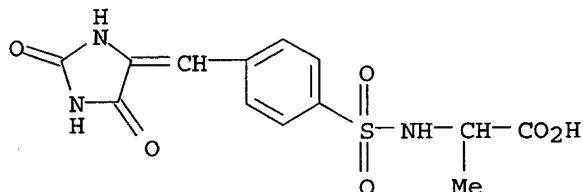
I

AB 5-Benzylidenehydantoin reacts with chlorosulfonic acid to give the corresponding p-sulfonyl chloride, I (R = Cl). Condensation of I (R = Cl) with amino acids leads to sulfonylamino acid derivs., which on coupling with glycine Me ester hydrochloride in THF-Et3N using the dicyclohexylcarbodiimide method furnish the desired dipeptide Me esters. The spectral data of the compds. are briefly discussed.

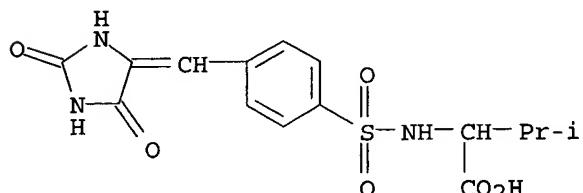
IT 331628-10-5P 331628-11-6P 331628-15-0P
 331628-17-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and reaction with glycine Me ester hydrochloride)
 RN 331628-10-5 HCAPLUS
 CN Glycine, N-[(4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl)sulfonyl]-
 (9CI) (CA INDEX NAME)



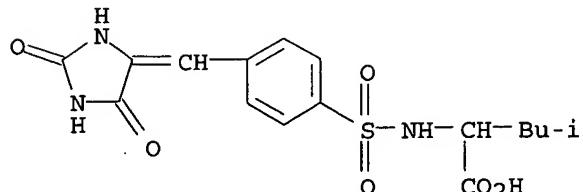
RN 331628-11-6 HCAPLUS
 CN Alanine, N-[(4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl)sulfonyl]-
 (9CI) (CA INDEX NAME)



RN 331628-15-0 HCAPLUS
 CN Valine, N-[(4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl)sulfonyl]-
 (9CI) (CA INDEX NAME)

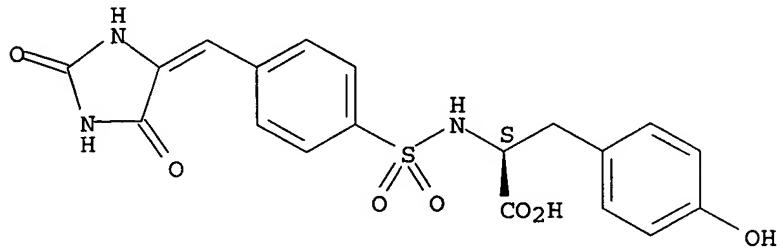


RN 331628-17-2 HCAPLUS
 CN Leucine, N-[(4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl)sulfonyl]-
 (9CI) (CA INDEX NAME)

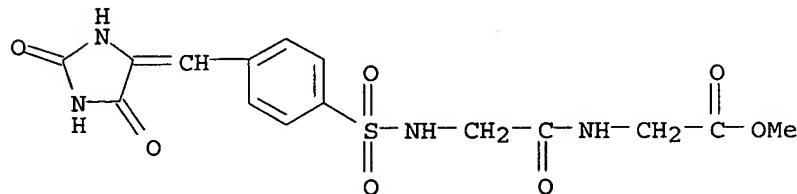


IT 331628-19-4P 331628-20-7P 331628-21-8P
 331628-22-9P 331628-24-1P 331628-26-3P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 331628-19-4 HCAPLUS
 CN L-Tyrosine, N-[(4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl)sulfonyl]
]- (9CI) (CA INDEX NAME)

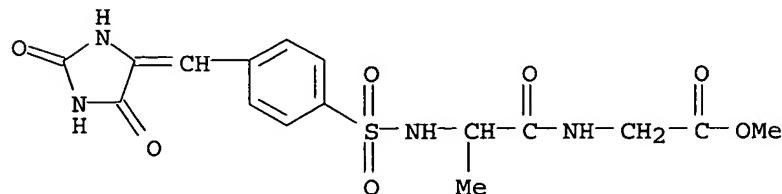
Absolute stereochemistry.
 Double bond geometry unknown.



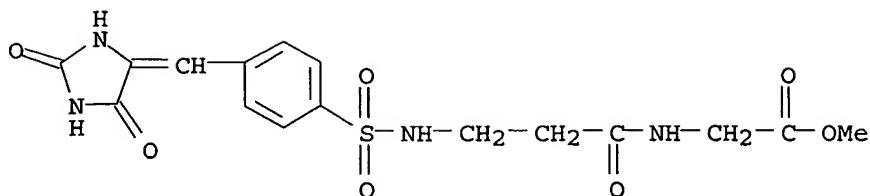
RN 331628-20-7 HCAPLUS
 CN Glycine, N-[(4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl)sulfonyl]glycyl-, methyl ester (9CI) (CA INDEX NAME)



RN 331628-21-8 HCAPLUS
 CN Glycine, N-[(4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl)sulfonyl]alanyl-, methyl ester (9CI) (CA INDEX NAME)

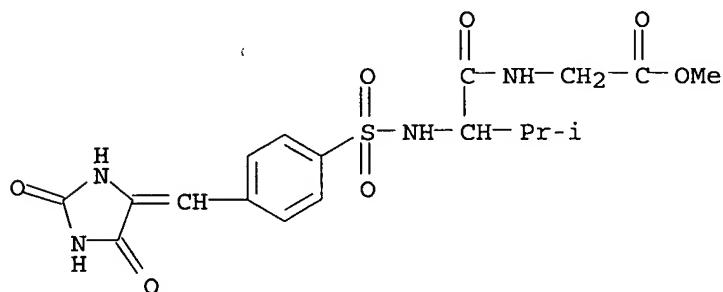


RN 331628-22-9 HCAPLUS
 CN Glycine, N-[(4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl)sulfonyl]-beta-alanyl-, methyl ester (9CI) (CA INDEX NAME)



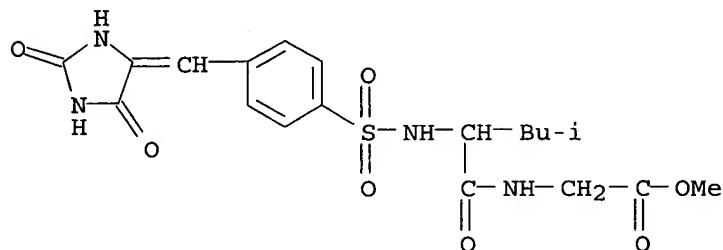
RN 331628-24-1 HCAPLUS

CN Glycine, N-[(4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl)sulfonyl]valyl-, methyl ester (9CI) (CA INDEX NAME)



RN 331628-26-3 HCAPLUS

CN Glycine, N-[(4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl)sulfonyl]leucyl-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:94908 HCAPLUS

DOCUMENT NUMBER: 134:252647

TITLE: Sulfur containing activated hydantions. Synthesis and screening some novel benzylidenehydantoins amino acids derivatives

AUTHOR(S): El-Sayed, Ragab A.

CORPORATE SOURCE: Chemistry Department, Faculty of Science, Al-Azhar University, Nasr City, Egypt

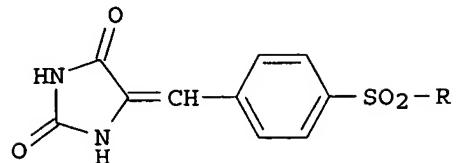
SOURCE: Journal of the Serbian Chemical Society (2001), 66(1), 17-21

CODEN: JSCSEN; ISSN: 0352-5139
PUBLISHER: Serbian Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE:
OTHER SOURCE(S):
GI

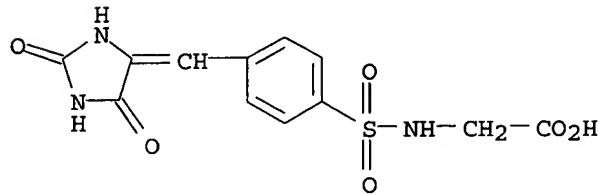
English
CASREACT 134:252647



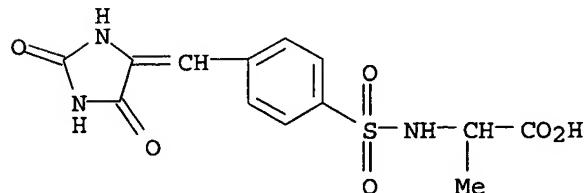
AB 5-Benzylidenehydantoin reacted with chlorosulfonic acid to give sulfonyl chloride I (R = Cl). Its condensation with amino acids gave N-(benzylidenehydantoin sulfonyl) amino acids I (R = Gly-OH, DL-Ala-OH, DL-Val-OH, DL-Leu-OH, β -Ala-OH, L-Tyr-OH). Coupling reactions of some of the above amino acid derivs. with H-Gly-OMe-HCl in a THF-Et3N medium using the dicyclohexylcarbodiimide (DCC) method provided dipeptide Me esters I (R = Gly-Gly-OMe, DL-Ala-Gly-OMe, β -Ala-Gly-OMe, DL-Val-Gly-OMe, DL-Leu-Gly-OMe). NMR and IR data of the synthesized compds. were briefly discussed.

IT 331628-10-5P 331628-11-6P 331628-15-0P
331628-17-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzylidenehydantoin sulfonyl derivs. of amino acids and dipeptides)

RN 331628-10-5 HCPLUS
CN Glycine, N-[[4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl]sulfonyl]-(9CI) (CA INDEX NAME)

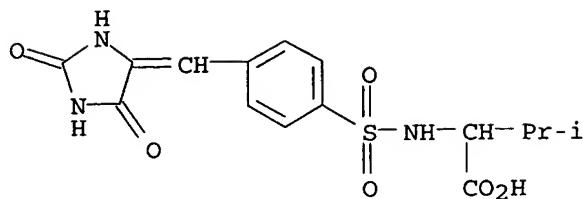


RN 331628-11-6 HCPLUS
CN Alanine, N-[[4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl]sulfonyl]-(9CI) (CA INDEX NAME)



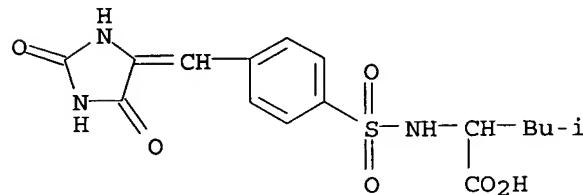
RN 331628-15-0 HCPLUS
CN Valine, N-[[4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl]sulfonyl]-

(9CI) (CA INDEX NAME)



RN 331628-17-2 HCAPLUS

CN Leucine, N-[(4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl)sulfonyl]-(9CI) (CA INDEX NAME)



IT 331628-19-4P 331628-20-7P 331628-21-8P

331628-22-9P 331628-24-1P 331628-26-3P

RL: SPN (Synthetic preparation); PREP (Preparation)

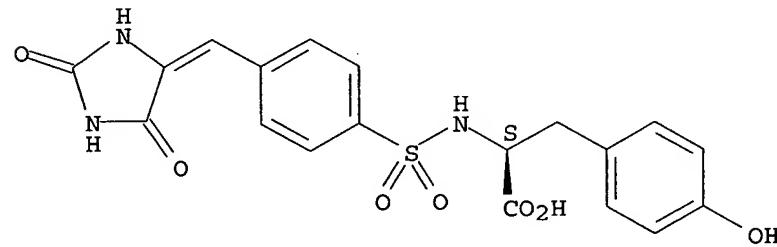
(preparation of benzylidenehydantoinsulfonyl derivs. of amino acids and dipeptides)

RN 331628-19-4 HCAPLUS

CN L-Tyrosine, N-[[4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

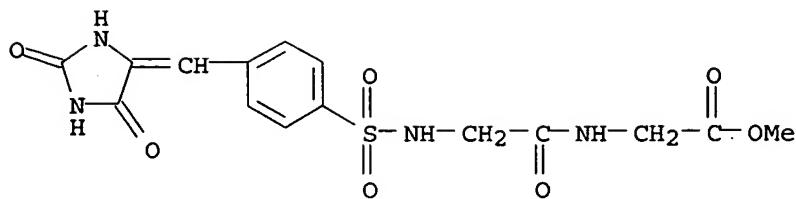
Absolute stereochemistry.

Double bond geometry unknown.

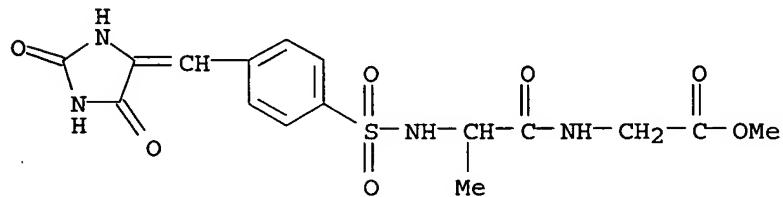


RN 331628-20-7 HCAPLUS

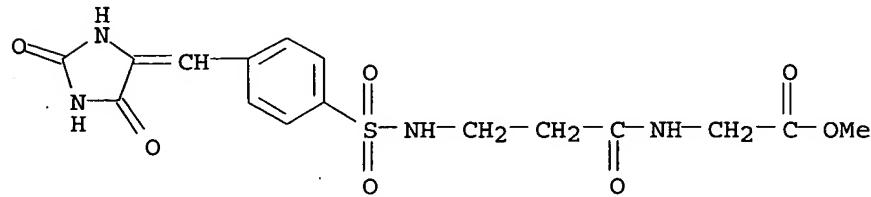
CN Glycine, N-[(4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl)sulfonyl]glycyl-, methyl ester (9CI) (CA INDEX NAME)



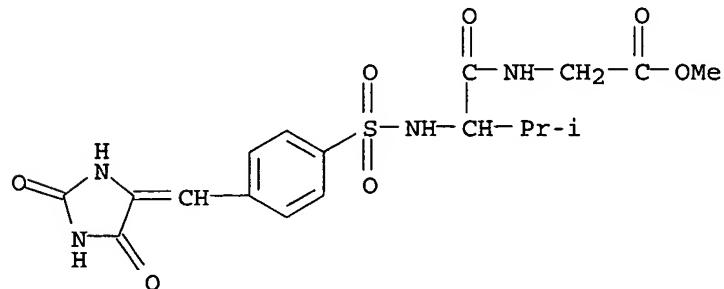
RN 331628-21-8 HCAPLUS
 CN Glycine, N-[(4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl)sulfonyl]alanyl-, methyl ester (9CI) (CA INDEX NAME)



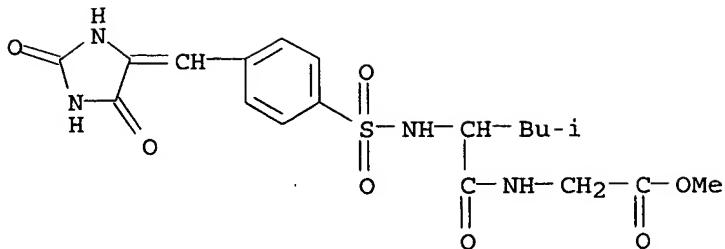
RN 331628-22-9 HCAPLUS
 CN Glycine, N-[(4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl)sulfonyl]beta-alanyl-, methyl ester (9CI) (CA INDEX NAME)



RN 331628-24-1 HCAPLUS
 CN Glycine, N-[(4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl)sulfonyl]valyl-, methyl ester (9CI) (CA INDEX NAME)



RN 331628-26-3 HCAPLUS
 CN Glycine, N-[(4-[(2,5-dioxo-4-imidazolidinylidene)methyl]phenyl)sulfonylleucyl-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 10 HCPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:15004 HCPLUS

DOCUMENT NUMBER: 132:73666

TITLE: Ophthalmic uses of PPAR- γ agonists and antagonists

INVENTOR(S): Pershadsingh, Harrihar A.; Levy, Daniel E.

PATENT ASSIGNEE(S) : Photogenesis, Inc., USA

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE: **Patent**

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT INFORMATION:

PATENT NO.

PATENT NO.	TYPE	DATE	INVENTION NO.	DATE
WO 2000000194	A1	20000106	WO 1999-US14262	19990625
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9947134	A1	20000117	AU 1999-47134	19990625
US 6316465	B1	20011113	US 1999-342381	19990628
RITY APPLN. INFO.:				
			US 1998-90937P	P 19980627
			US 1998-90937	P 19980627
			WO 1999-US14262	W 19990625

OTHER SOURCE(S) : MARPAT 132:73666

AB Methods are disclosed for treating diseases of ocular tissues expressing the nuclear receptor PPAR- γ , by inhibiting the inflammatory response, the neovascularization and angiogenesis, and programmed cell death (apoptosis) in these target tissues, comprising administering to a human or animal in need of treatment an effective amount of a compound that modifies the activity of PPAR- γ , or a pharmaceutically acceptable salt or solvate thereof. Novel compds. and methods for their synthesis are provided.

IT 253587-89-2 253587-91-6 253587-93-8

253587-96-1

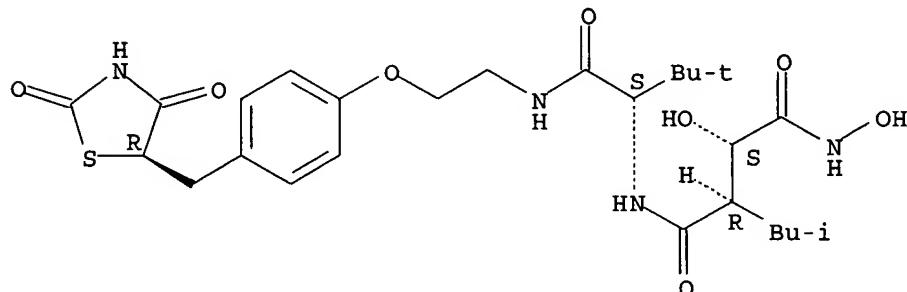
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ophthalmic uses of PPAR- γ agonists and antagonists)

RN 253587-89-2 HCPLUS

CN Butanediamide, N4-[(1S)-1-[[[2-[4-[(5R)-2,4-dioxo-5-thiazolidinyl]methyl]phenoxy]ethyl]amino]carbonyl]-2,2-dimethylpropyl-N1,2-dihydroxy-3-(2-methylpropyl)-, (2S,3R)- (9CI) (CA INDEX NAME)

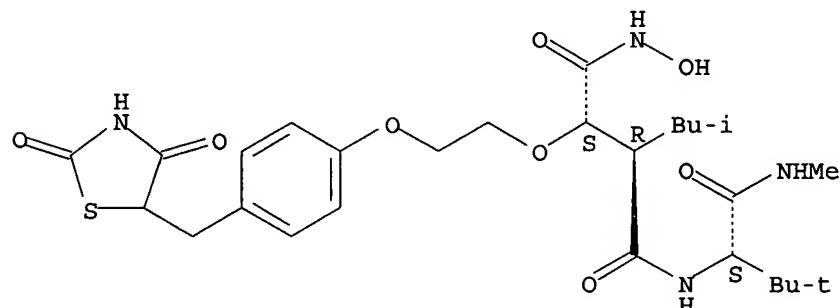
Absolute stereochemistry.



RN 253587-91-6 HCPLUS

CN Butanediamide, N4-[(1S)-2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-2-[2-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]ethoxy]-N1-hydroxy-3-(2-methylpropyl)-, (2S,3R)- (9CI) (CA INDEX NAME)

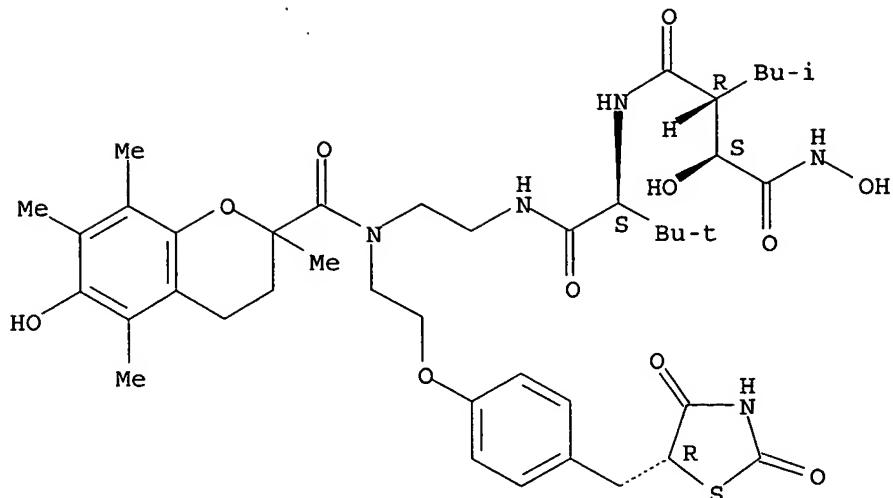
Absolute stereochemistry.



RN 253587-93-8 HCPLUS

CN Butanediamide, N4-[(1S)-1-[[[2-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)carbonyl] [2-[4-[(5R)-2,4-dioxo-5-thiazolidinyl]methyl]phenoxy]ethyl]amino]ethyl]amino]carbonyl]-2,2-dimethylpropyl-N1,2-dihydroxy-3-(2-methylpropyl)-, (2S,3R)- (9CI) (CA INDEX NAME)

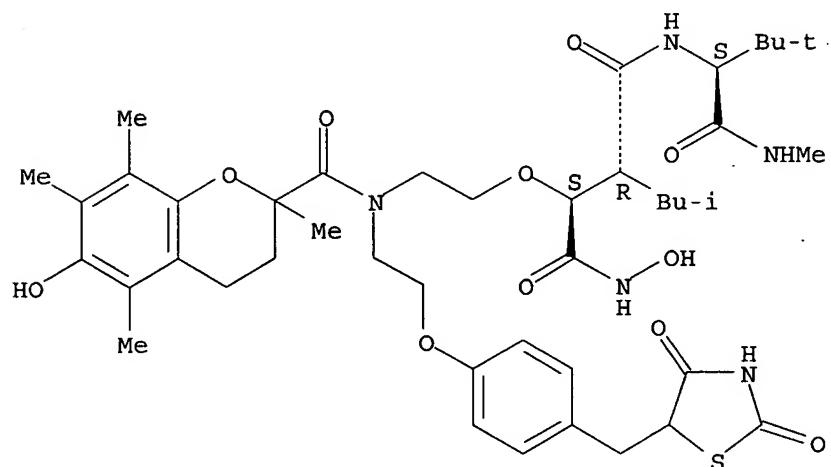
Absolute stereochemistry.



RN 253587-96-1 HCAPLUS

CN Butanediamide, 2-[2-[[[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)carbonyl][2-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]ethyl]amino]ethoxy]-N4-[(1S)-2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1-hydroxy-3-(2-methylpropyl)-, (2S,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:743595 HCAPLUS

DOCUMENT NUMBER: 126:19325

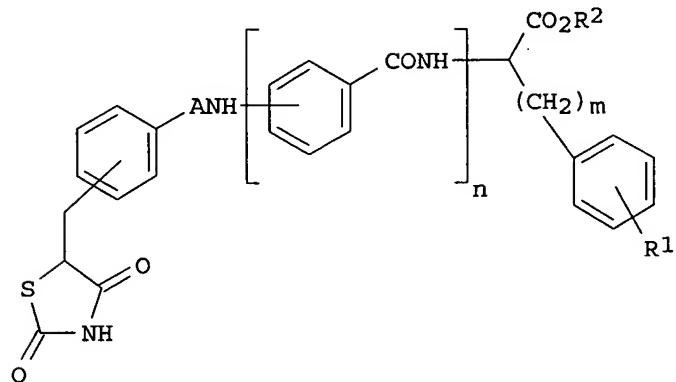
TITLE: Preparation of (dioxothiazolidinylalkylbenzoyl)phenylalanine derivatives and analogs as hypoglycemics and aldose reductase inhibitors

INVENTOR(S): Matsushima, Hiroaki; Myaoka, Shozo; Sugizaki, Myoshi
PATENT ASSIGNEE(S): Terumo Corp, Japan

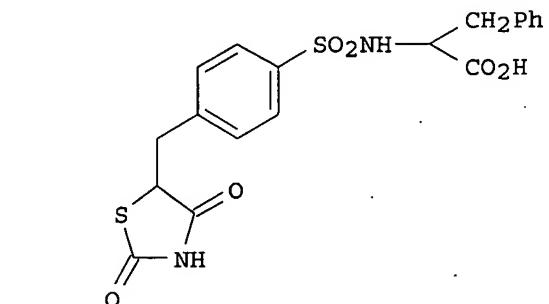
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.

DOCUMENT TYPE: CODEN: JKXXAF
 LANGUAGE: Patent
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08245602	A2	19960924	JP 1995-48022	19950308
PRIORITY APPLN. INFO.:			JP 1995-48022	19950308
OTHER SOURCE(S):	MARPAT 126:19325			
GI				



I



II

AB The title compds. I [A = carbonyl, etc.; R1 = H, halo; R2 = H, alkyl; m, n = 0 or 1] are prepared Dioxothiazolidine derivative II (preparation given) in vitro

showed IC50 of 6.35×10^{-6} M against aldose reductase.

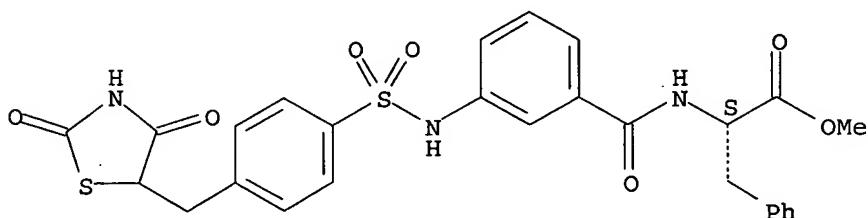
IT 184095-73-6P 184095-74-7P 184095-75-8P
 184095-76-9P 184095-77-0P 184095-78-1P
 184095-79-2P 184095-80-5P 184095-81-6P
 184095-82-7P 184095-84-9P 184095-85-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of (dioxothiazolidinylalkylbenzoyl)phenylalanine derivs. and analogs as hypoglycemics and aldose reductase inhibitors)

RN 184095-73-6 HCPLUS

CN L-Phenylalanine, N-[3-[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]sulfonyl]amino]benzoyl-, methyl ester (9CI) (CA INDEX NAME)

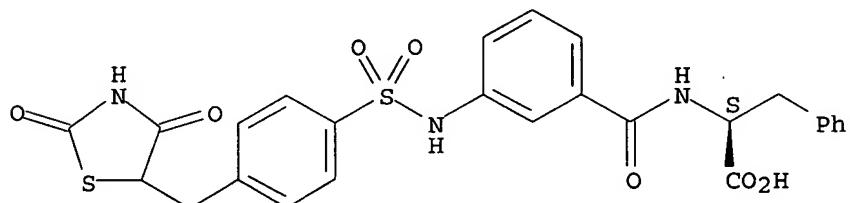
Absolute stereochemistry.



RN 184095-74-7 HCPLUS

CN L-Phenylalanine, N-[3-[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]sulfonyl]amino]benzoyl- (9CI) (CA INDEX NAME)

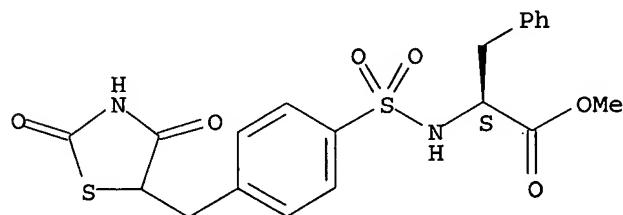
Absolute stereochemistry.



RN 184095-75-8 HCPLUS

CN L-Phenylalanine, N-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]sulfonyl-, methyl ester (9CI) (CA INDEX NAME)

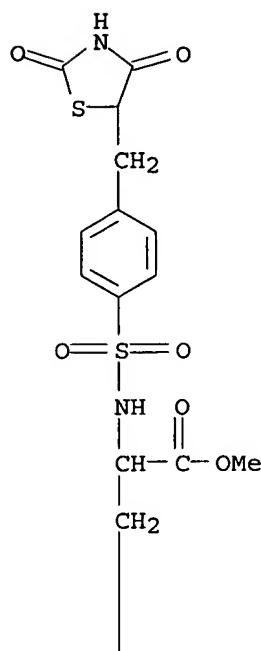
Absolute stereochemistry.



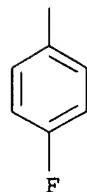
RN 184095-76-9 HCPLUS

CN Phenylalanine, N-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]sulfonyl]-4-fluoro-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



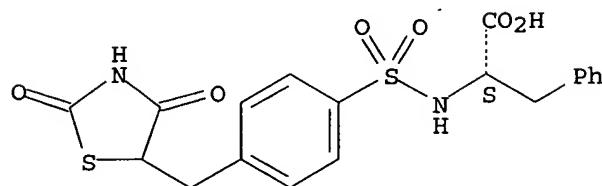
PAGE 2-A



RN 184095-77-0 HCPLUS

CN L-Phenylalanine, N-[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

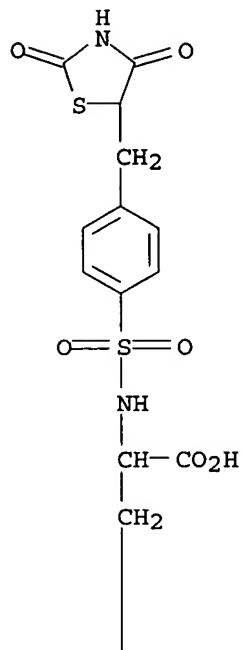
Absolute stereochemistry.



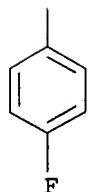
RN 184095-78-1 HCPLUS

CN Phenylalanine, N-[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]sulfonyl]-4-fluoro- (9CI) (CA INDEX NAME)

PAGE 1-A

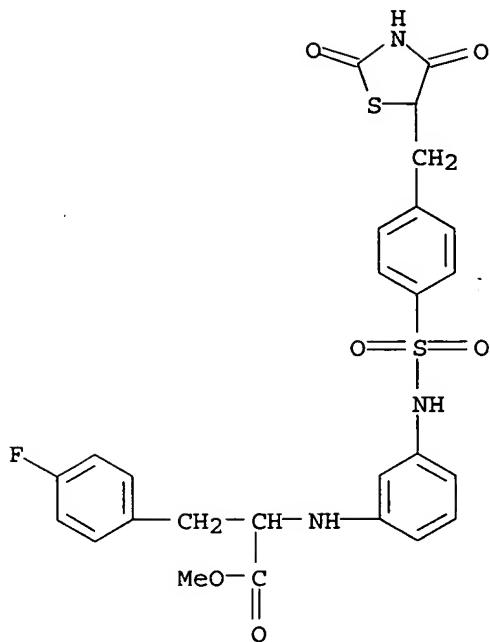


PAGE 2-A



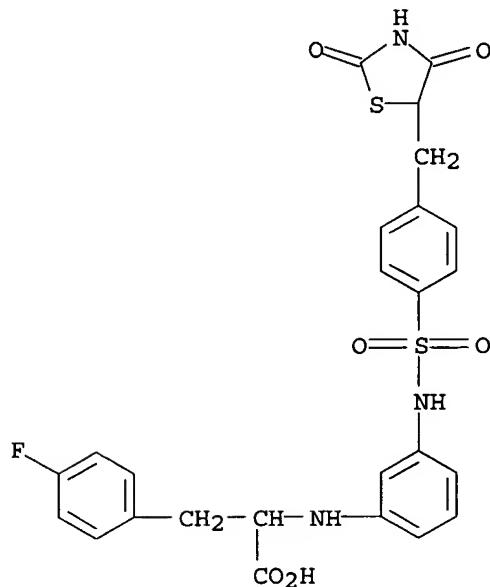
RN 184095-79-2 HCPLUS

CN Phenylalanine, N-[3-[[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]sulfonyl]amino]phenyl]-4-fluoro-, methyl ester (9CI) (CA INDEX NAME)



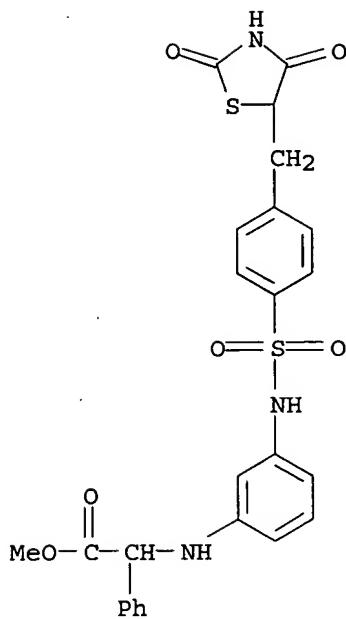
RN 184095-80-5 HCPLUS

CN Phenylalanine, N-[3-[[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]sulfonyl]amino]phenyl]-4-fluoro- (9CI) (CA INDEX NAME)

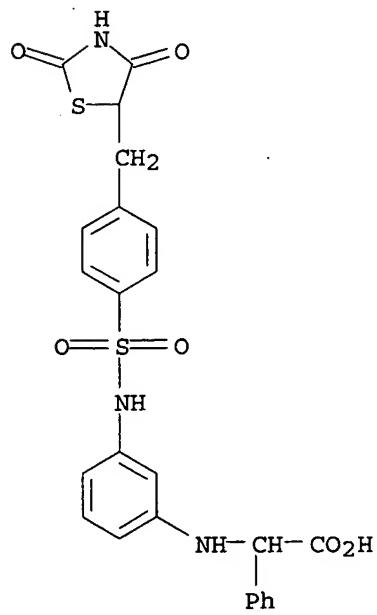


RN 184095-81-6 HCPLUS

CN Benzeneacetic acid, α -[[3-[[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]sulfonyl]amino]phenyl]amino]-, methyl ester (9CI) (CA INDEX NAME)

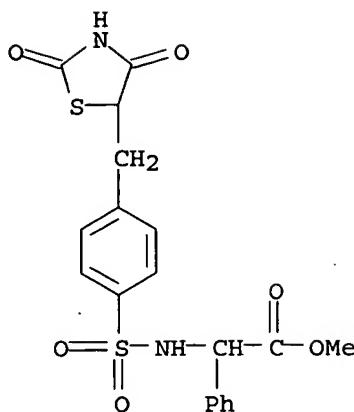


RN 184095-82-7 HCAPLUS

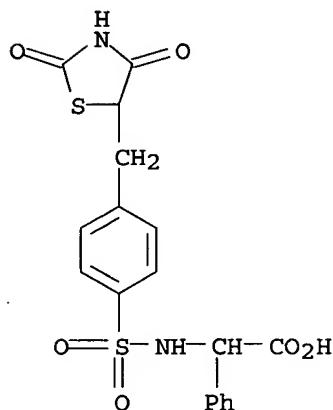
CN Benzeneacetic acid, α -[[3-[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]sulfonyl]amino]phenyl]amino]- (9CI) (CA INDEX NAME)

RN 184095-84-9 HCAPLUS

CN Benzeneacetic acid, α -[[3-[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]sulfonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)



RN 184095-85-0 HCAPLUS

CN Benzeneacetic acid, α -[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]sulfonyl]amino]- (9CI) (CA INDEX NAME)

L7 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2005 ACS on STM

ACCESSION NUMBER: 1983:125945 HCAPLUS

DOCUMENT NUMBER: 98:125945

TITLE: Studies on antidiabetic agents. II. Synthesis of 5-[4-(1-methylcyclohexylmethoxy)benzyl]thiazolidine-2,4-dione (ADD-3878) and its derivatives.

AUTHOR(S): Sohda, Takashi; Mizuno, Katsutoshi; Imamiya, Eiko; Sugiyama, Yasuo; Fujita, Takeshi; Kawamatsu, Yutaka

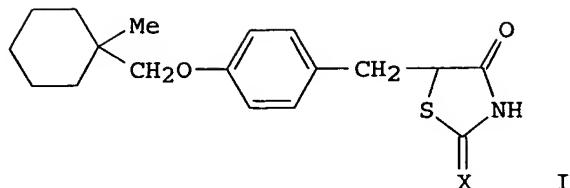
CORPORATE SOURCE: Cent. Res. Div., Takeda Chem. Ind., Ltd., Osaka, 532, Japan

SOURCE: Chemical & Pharmaceutical Bulletin (1982), 30(10), 3580-600

DOCUMENT TYPE: CODEN: CPBTAL; ISSN: 0009-2363

LANGUAGE: English

GI



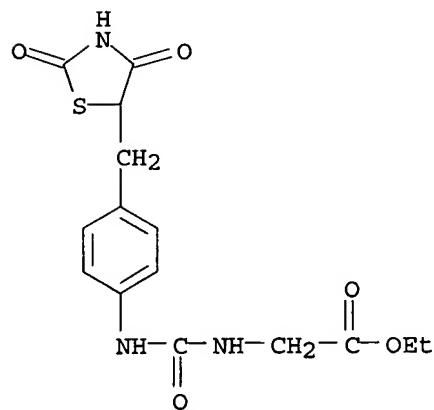
AB More than 100 5-substituted thiazolidine-2,4-diones were prepared and their hypoglycemic and hypolipidemic activities were evaluated with genetically obese and diabetic mice, yellow KK. Thus, 2-chloro-3-[4-(1-methylcyclohexylmethoxy)phenylpropionate was cyclized with H₂NCSNH₂ to give the thiazolidinone I (X = NH), which was hydrolyzed to give I (X = O). The structure-activity relationship study showed that the 5-(4-oxybenzyl) moiety is essential for substantial activity. Among these compds., 5-(4-cyclohexylmethoxy)benzylthiazolidine-2,4-dione I (X = O) and 5-[4-[2-(3-pyridyl)ethoxy]benzyl]thiazolidine exhibited the most favorable properties in terms of activity and toxicity.

IT 85002-42-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and hypoglycemic and hypolipidemic activity of)

RN 85002-42-2 HCPLUS

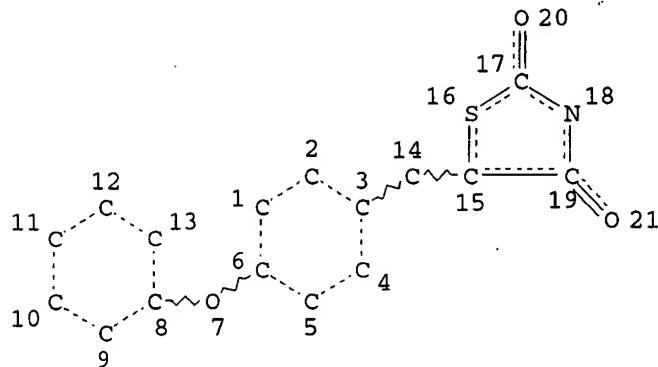
CN Glycine, N-[[[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]amino]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)



=> d que 121

L17

STR



NODE ATTRIBUTES:

CONNECT IS E3 RC AT 11

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

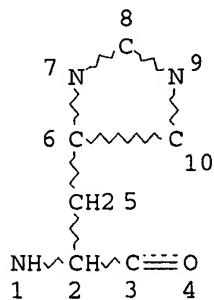
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

L19 40 SEA FILE=MARPAT SSS FUL L17

L20 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

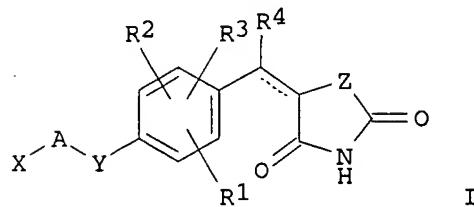
L21 1 SEA FILE=MARPAT SUB=L19 SSS FUL L20

=> d 121 ibib abs qhit

L21 ANSWER 1 OF 1 MARPAT COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 141:140764 MARPAT
 TITLE: Preparation of amino acid phenoxy ethers as inhibitors
 of cytokines
 INVENTOR(S): Nag, Bishwajit; Nag, Abhijeet; Dey, Debendranath;
 Agarwal, Shiv Kumar
 PATENT ASSIGNEE(S): Bexel Pharmaceuticals, Inc., USA
 SOURCE: U.S. Pat. Appl. Publ., 47 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004142991	A1	20040722	US 2003-356113	20030131
US 6794401	B2	20040921		
WO 2004066964	A2	20040812	WO 2004-US790	20040113
WO 2004066964	C2	20040902		
WO 2004066964	A3	20050224		
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
PRIORITY APPLN. INFO.:			US 2003-440772P	20030117
			US 2003-356113	20030131

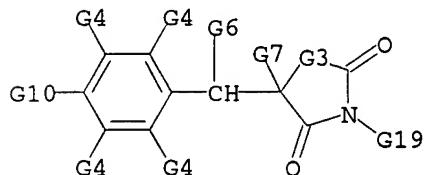
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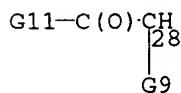
AB Novel amino acid Ph ethers, e.g. tyrosine Ph ethers, or tautomeric forms, stereoisomers, polymorphs, pharmaceutically acceptable salts, or pharmaceutically acceptable solvates thereof [I; wherein the dotted line represents an optional double bond; Y = O, S, NR (wherein R represents hydrogen or alkyl); Z = O, S; R1-R4 = H, halogen, HO, nitro, cyano, formyl, amino, alkyl, alkoxy; A = a bond or substituted or unsubstituted aryl, heterocyclyl or heteroaryl ring; X = an alpha aminocarboxylic acid or alpha aminocarboxylic acid derivative bonded to A or Y through its alpha side chain] are prepared. Also provided are a method for reducing glucose, free fatty acids, cholesterol, or triglyceride levels in plasma. These compds. inhibit cytokines such as TNF α , IL-6, and IL-1 β and

exhibit activity for the treatment of immunol. diseases mediated by cytokines, autoimmune diseases such as multiple sclerosis and rheumatoid arthritis, inflammation mediated by cyclooxygenase, obesity, hyperlipidemia, hypertension, neurol. diseases and diabetes, or a disorder associated with insulin resistance. Unlike other thiazolidine-compds. (TZD mols.), the compds. I exhibit no adipocyte differentiation, reduce body weight gain, and appear to have no affinity for PPAR- γ and thereby are different from known TZD mols., which typically have adipocyte differentiation activity, increase weight gain, and are PPAR- γ agonists. Thus, Me 2-[(tert-butoxycarbonyl)amino]-3-(4-hydroxyphenyl)propanoate was treated with NaH in DMF and etherified with 4-Fluorobenzaldehyde at 80° to give Me 2-[(tert-butoxycarbonyl)amino]-3-[-(4-formylphenoxy)phenyl]propanoate which was condensed with 2,4-thiazolidinedione in the presence of benzoic acid and piperidine at 145-155° under reflux with continuous removal of water using Dean-Stark apparatus for 5 h followed by treatment with HCl in CH₂Cl₂ to give 5-[4-[4-(2-amino-2-methoxycarbonyl)phenoxy]benzylidene]thiazolidine-2,4-dione hydrochloride (II). Catalytic hydrogenation of II over Pd/C in methanol gave 5-[4-[4-(2-amino-2-methoxycarbonyl)phenoxy]benzyl]thiazolidine-2,4-dione (III). III lowered pro-inflammatory cytokines in human macrophage cells and in an animal model of inflammation inhibited carrageenan-induced paw edema in SD rats.

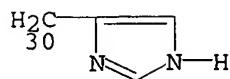
MSTR 1



G1 = NH
G8 = 28



G9 = 30

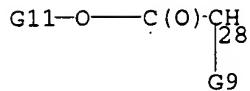


MPL: claim 1
NTE: and tautomers, polymorphs, and pharmaceutically acceptable solvates
STE: and stereoisomers

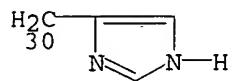
MSTR 2

G10—H

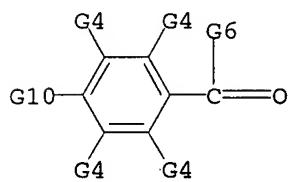
G1 = NH
 G8 = 28



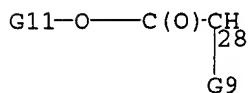
G9 = 30



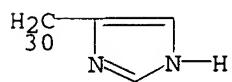
MPL: claim 18

MSTR 3

G1 = NH
 G8 = 28

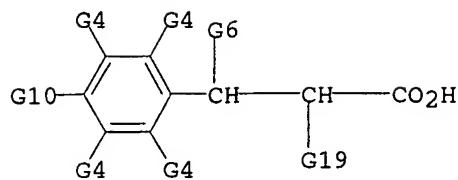


G9 = 30

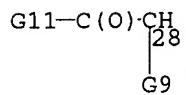


MPL: claim 18

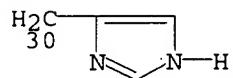
MSTR 4



G1 = NH
G8 = 28



G9 = 30



MPL: claim 19

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT